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Dissertation

Dynamic stability control and human energetics

Dissertation

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Zusammenfassung

Die Bewegungs-kontrollstrategien kontextabhängig und abhängig von unterschiedlichen Kriterien ausgewählt werden. Einerseits ist die Stabilität in den Bewegungszuständen wie der Fortbewegung ausschlaggebend für die ungestörte Ausführung bestimmter Handlungen und erfordert eine effektive Steuerung durch das zentrale Nervensystem. Andererseits wird die Bewegungsstrategieauswahl durch das zentrale Nervensystem dadurch bestimmt, dass die Energiekosten minimiert werden soll. Beide Konzepte (d.h. die Aufrechterhaltung der Stabilität und die Energiekostenminimierung) spielen eine fundamentale Rolle bei der Frage, warum sich Menschen so bewegen, wie sie es tun. Unklar ist dabei allerdings, auf welche Weise das zentrale Nervensystem beide Prinzipien gegeneinander gewichtet.

In den letzten 20 Jahren haben uns wissenschaftliche Konzepte wie die Chaostheorie oder die Theorie komplexer Systeme eine neue Herangehensweise an diese Fragen ermöglicht. Diese Arbeit untersucht die dynamische Stabilität menschlicher Fortbewegung mit Hilfe des Konzepts der Ljapunowanalyse. Als erstes wird eine methodologische Untersuchung der Verlässlichkeit des maximalen Ljapunowexponenten beim Gehen und Laufen durchgeführt (Kapitel 2). Danach wird verglichen zwischen dem Laufen unter normalen Umständen und dem darauffolgenden Laufen ohne Schuhe, wobei letzteres eine Abnahme der Stabilität nach dem Übergang zu den neuen Umständen zur Folge hat (Kapitel 3). In der letzten Untersuchung wurde ein unterschiedlich langes Training zur Verbesserung der Laufenergetik durchgeführt, in einer Gruppe nur über einen kurzen und in einer anderen Gruppe über einen etwas längeren Zeitraum (Kapitel 4). Die Ergebnisse zeigen, dass Bewegungskontrollfehler für die Energiekosten beim Laufen eine Rolle spielen können, und legen somit eine flexible Priorisierung der Bewegungskontrolle nahe.

Schlagwörter: Bewegungskontrolle, Dynamische Stabilität, Energiekosten, Ljapunowanalyse, zentrale Nervensystem, flexible Priorisierung, Lokomotion, Biomechanik, Neurowissenschaften

Abstract

Motor control strategies are chosen in a context dependent manner, based on different criteria. On the one hand stability in dynamic conditions such as locomotion, is crucial to uninterrupted task execution and requires effective regulation by the central nervous system. On the other, minimization of the energetic cost of transport is instrumental in choosing the locomotion strategy by the central nervous system. Both these concepts, (i.e. maintaining stability and optimization of energetic cost of locomotion) have a fundamental role on how and why humans move in the way they do. However, how the human central nervous system prioritizes between the different goals is unknown.

In the last 20 years, ideas from scientific paradigms such as chaos theory and complex systems have given us novel tools to approach these questions. The current thesis examines the dynamic stability during human locomotion under such an approach using the concept of Lyapunov analysis. At first a methodological examination of the reliability of the maximum Lyapunov exponent in walking and running has been conducted (chapter 2). Afterwards, an examination between the habitual running condition and after removal of footwear was conducted, exhibiting a decrease in stability following the acute transition to the new condition (chapter 3). In the last study, a training intervention aiming at improvements in running energetics was performed using a short-term and a long-term intervention group (chapter 4). The results evidence that motor control errors can have a role in the energy cost of running and thus, a flexible prioritization of the motor control output.

Keywords: Motor control, dynamic stability, energy cost, Lyapunov analysis, central nervous system, flexible prioritization, locomotion, biomechanics, neuroscience

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Curriculum Vitae ..... Error! Bookmark not defined.

To my grandparents

for their perseverance in face of hardships
and will to improve everything around them

1 Introduction

The greatest scientific discovery was the discovery of ignorance.

Yuval Noah Harari, 2017[1]

Humans remain biologically novel among other animals in several aspects such as language, dexterity and complex culture. However, while two legged locomotion is common in animal species, the manner in which humans stand, walk and run is observed only in our species[2]. The unique features of human locomotion attracted the interest of early philosophers such as Aristotle (384–322 BC), to whom the influential writing "Περὶ ζῴων κινήσεως" (On the Gait of Animals) is attributed. An infamous quote of the book reads: "If a man were to walk parallel to a wall in sunshine, the line described (by the shadow of his head) would be not straight but zigzag, becoming lower as he bends, and higher when he stands and lifts himself up." Aristotle (as translated by Farquharson, 2007)[3].

Understanding the mechanics of human locomotion is important to interpret the adaptive evolution of our species, rehabilitate dysfunctional movement patterns, maximize performance and prevent injuries[3]. In the last 20 years, ideas from scientific paradigms such as chaos theory and complex systems have been integrated with concepts and tools from dynamical systems theory to re-shape the understanding of movement behaviour[4,5]. The current thesis examines the dynamic stability during human locomotion under such an approach using the concept of Lyapunov analysis.

On one hand, during locomotion stability represents a *sine qua non* concept. On the other, minimization of the energetic cost of transport is instrumental in choosing the locomotion strategy by the central nervous system. Both these concepts, (i.e. maintaining stability and optimization of energetic cost) have a fundamental role on how and why humans move in the way they do. Current knowledge in human locomotion remains opaque in regard to how these concepts interact and influence the movement strategies in humans suggesting the existence of an exciting window for research.

The present chapter will endeavour to present the current knowledge in the respective fields along with parts of historical, methodological and computational interest. The experimental

part of this thesis will be presented in the following three chapters. It will conclude in the fourth and last chapter with a summary of the main findings and how these can lead to advances in the bio- and neuromechanics or related fields.

1.1 Dynamical systems

Dynamics in the grander scheme of mathematics refer to the study of change, or how a system evolves over time. The concept of a dynamical system has its origins in Newtonian mechanics. A dynamical system must follow mathematical formalizations (i.e. fixed rules) that describe its evolution over time or the time dependence of a point in a geometrical space. Dynamical systems can be found in various fields (e.g. classical mechanics, chemistry, biology) and popular examples include the swinging of a clock pendulum, the flow of water in a pipe and the growth of a bacteria population. Although dynamics is an interdisciplinary subject today, it was originally a branch of physics. The subject began in the mid-1600s, when Newton invented differential equations, discovered the laws of motion and universal gravitation, and combined them to explain Kepler's laws of planetary motion[6]. In Table 1 the progression of analysis in dynamical systems is presented.

During the evolution through time, a system can be described based on its state; a vector of real numbers representing a point in the appropriate n-dimensional geometrical manifold. Based on this approach, a clear mathematical definition to dynamical systems can now be given. A dynamical system is a rule for time evolution on a state space, where a state space represents the set of all possible states of the dynamical system. Such a system can settle to equilibrium, keep repeating in cycles or do something more complicated[6]. A trajectory is a time-ordered set of states of a dynamical system and geometrically represents a path in the state space. The evolution rule determines what future states follow the current state. Determining the state for all future times in a dynamical system requires iterating the governing relation of the system many times, advancing time a small step at a time. Dynamical systems are deterministic if there is a unique consequent state to every given state, or stochastic if there is a probability distribution of possible consequent states.

Knowing how the trajectory path behaves in simple systems is sufficient to understand the behavior of the system and predict its future states. However, more complex systems are often impossible to be understood or approximated in terms of individual trajectories. This is how the notion of stability has been introduced into the study of the dynamical systems.

Table 1. The progression of analysis in dynamical systems (adapted from Strogatz 1994)[6]

1666	Newton	Invention of calculus, explanation of planetary motion
1700s		Flowering of calculus and classical mechanics
1800s		Analytical studies of planetary motion
1890s	Poincare	Geometric approach, nightmares of chaos
1920-1950		Nonlinear oscillators in physics and engineering, invention of radio, radar, laser
1920-1960	Birkhoff	Complex behavior in Hamiltonian mechanics
	Kolmogorov	
	Arnol'd	
	Moser	
1963	Lorenz	Strange attractor in simple model of convection
1970s	Ruelle &Takens	Turbulence and chaos
	May	Chaos in logistic map
	Feigenbaum	Universality and renormalization, connection between chaos and phase transitions
		Experimental studies of chaos
	Winfree	Nonlinear oscillators in biology
	Mandelbrot	Fractals
1980s		Widespread interest in chaos, fractals, oscillators, and their applications

This section will start by presenting the concept of stability in dynamical systems through a historical and overview perspective. It will then endeavor to present the calculation of the local dynamic stability of a system numerically, through the maximum Lyapunov exponent, starting from the transformation of data through state space reconstruction, the actual numerical estimation of the exponent and its associated properties.

1.1.1 Stability in dynamical systems

It was not long after the realization that the evolution of physical systems can be described in terms of mathematical equations, that the stability of the various dynamical regimes was recognized as a matter of primary importance. For instance, scientists needed to know in the 19th century, how would mechanical devices behave after their configuration have been perturbed. There are two dominant theoretical approaches of stability in dynamical systems; dynamic stability and structural stability.

The first who gave an exact definition on stability was the Russian mathematician Aleksandr Mikhailovich Lyapunov who addressed the problem in his PhD Thesis “The General Problem of Stability of Motion” at the Moscow University in 1892[7]. Lyapunov stability or dynamic stability considers perturbations of initial conditions for a fixed system and characterizes whether nearby (i.e., perturbed) orbits will remain in a neighborhood of that orbit or be repelled away from it. Dynamic stability in this construct indicates how the system reacts to a perturbation[7].

Before A. M. Lyapunov the widely spread method of analyzing stability was linearizing systems about the points of equilibrium. This new mathematical theory of stability of motion was much ahead of its time. Despite A. M. Lyapunov having significant contributions at the Fourth International Mathematical Congress in Rome and participating in the publication of Euler's selected works, his own work received little attention for many years. Decades passed until the theory of stability resurrects from complete oblivion by the Soviet mathematician Nikolay Gur'yevich Chetaev. His contribution to the theory was so significant that many mathematicians consider him the direct successor of Lyapunov and the next-in-line more important figure in the creation and development of the mathematical theory of stability[8]. During the Cold War, the "Second Method of Lyapunov" received enormous attention as it

was applicable to the stability of aerospace guidance systems. Such systems, typically contain strong nonlinearities, that are not treatable by other methods. The current thesis expands on the notion of local dynamic stability of dynamical systems measured through the maximum Lyapunov exponent.

The idea of Lyapunov stability can be extended to infinite-dimensional manifolds, where it converges to the notion of the structural stability. Structural stability was introduced by Andronov and Pontrjagin in 1937 and refers to changes in the family of all solutions due to perturbations to the functions defining the dynamical system itself[9–11]. As such, in the notion of structural stability the qualitative behavior of the trajectories is unaffected by small perturbations[9–11].

1.1.2 Maximum Lyapunov exponent

In time series analysis one tries to infer the internal variables of the system, such as its stability, by means of external measurements. Numerically calculating the local dynamic stability of system is not a trivial task. In achieving the optimal estimation of the maximum Lyapunov exponent of a system, a series of steps has to be performed.

1.1.2.1 State-space reconstruction

State-space reconstruction constitutes the foundation of the nonlinear time series analysis[12]. In 1980 and 1981, two pioneering papers laid the foundation for what became known as nonlinear time-series analysis: the analysis of observed data via dynamical systems theory. Based on the concept of state-space reconstruction, this set of methods allows to compute characteristic quantities such as Lyapunov exponents and fractal dimensions[12]. In mathematics, a space is a set (sometimes called a universe) with some added structure. A state space is an abstract space in which different "positions" represent, not literal locations, but rather states of some physical system. The foundations of state space reconstruction were initially laid by Packard et al. in the influential work “Geometry of a time series”[13]. Following, an important contribution was made through the *embedding theorem* formulated by Takens[14]. Under the *embedding theorem,* the structure of the original state space is

guaranteed to be represented from the space of time delayed vectors that have a sufficiently large dimension. The dimension of the state space of a dynamical system is also the number of degrees of freedom of the system, i.e., the number of variables that is needed to completely describe it. However, there is an upper bound provided for the embedding dimension[15]. In the context of Hamiltonian systems, the number of degrees of freedom is the number of pairs of state variables.

State space reconstruction of the dynamics of the system is numerically accomplished through delay-coordinate embedding. The initial input for the reconstruction can be as simple as a one-dimensional time series (Figure 1).

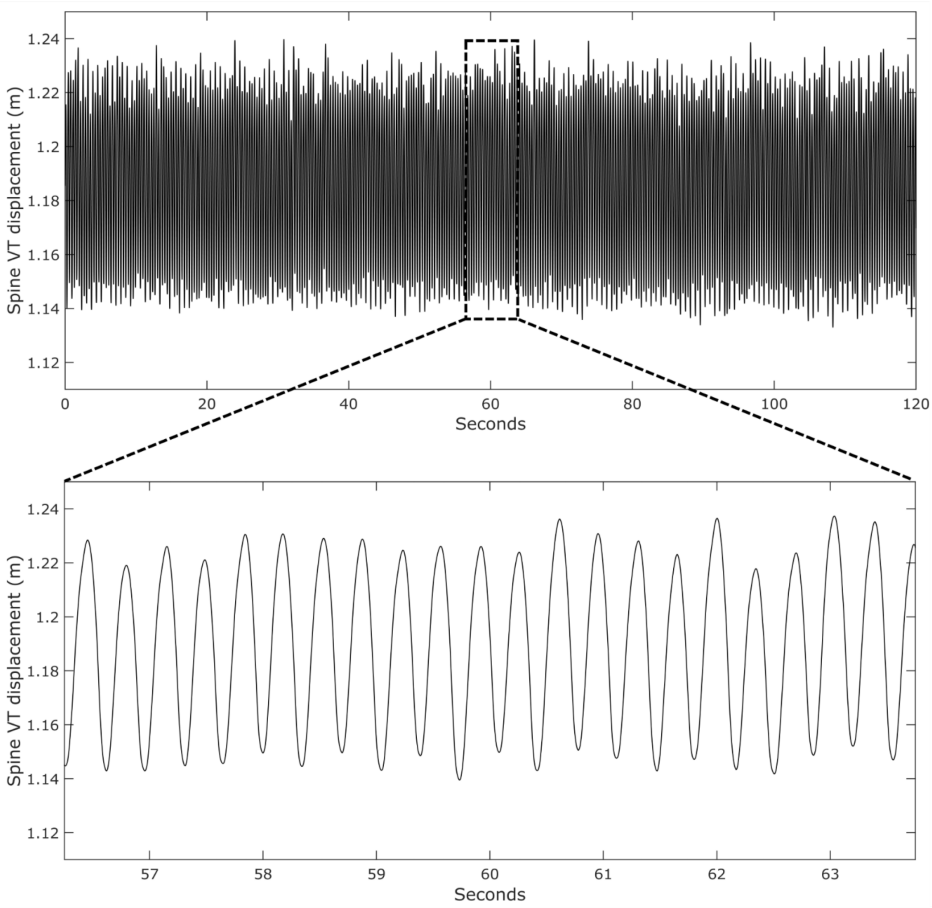

Figure 1. One dimensional time series used for subsequent analysis

The reconstruction is then performed on the given input data and time-delayed copies of each point in the time series[13,16,17] as follows:

$$\boldsymbol{S(t)} = [z(t), z(t+\tau), \ldots, z(t+(m-1)\tau)], \quad (1)$$

with **S(t)** being the *m*-dimensional reconstructed state vector, z(t) the input 1D coordinate series, τ the time delay and *m* the embedding dimension. Time delays are commonly calculated from the first minimum of the mutual-information curve extracted from the Average Mutual Information function[18]. The function quantifies the dependence -in terms of information- between two variables (i.e. whether the value of one variable can be predicted given knowledge of the other)[19,20]. The Average Mutual Information of sets of measurements $I(X,Y)$, can be given from the following equation:

$$I(X,Y) = \int\int p(x,y) ln \frac{p(x,y)}{p(x)p(y)} dxdy \quad (2)$$

In Figure 2 the Average Mutual Information is plotted against different delay values. The vertical line indicates the first minimum of the function.

The number of embedding dimension is commonly calculated through a Global False Nearest Neighbors analysis[21] for the given time series. Figure 3 shows how the percentage of false neighbors is changing based on the choice of different embedding dimensions.

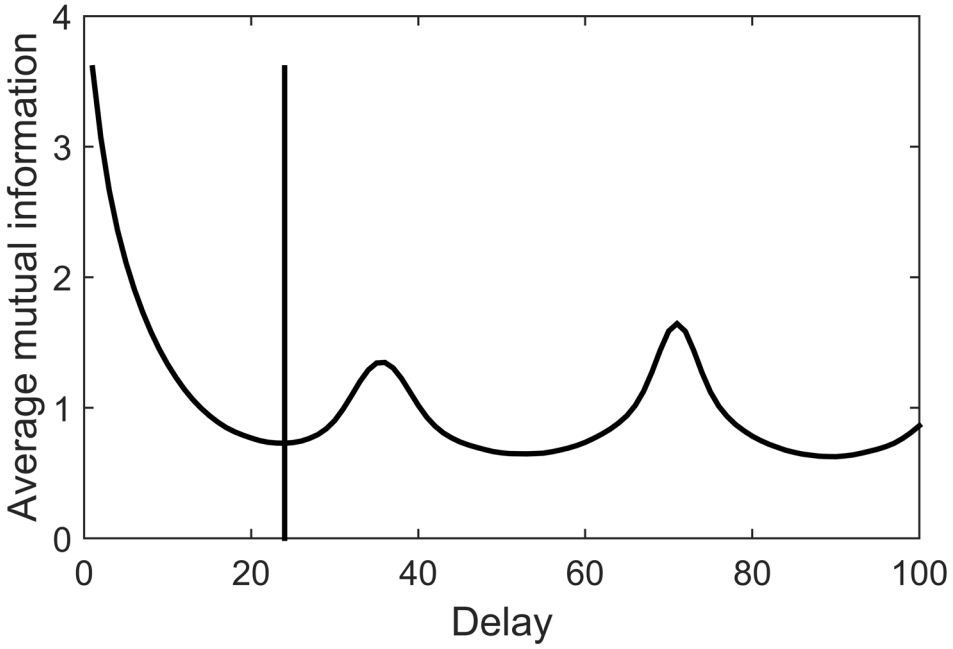

Figure 2. The average mutual information function when using different values of delay. The vertical line depicts the chosen numerical value of delay given by the first minimum of the function.

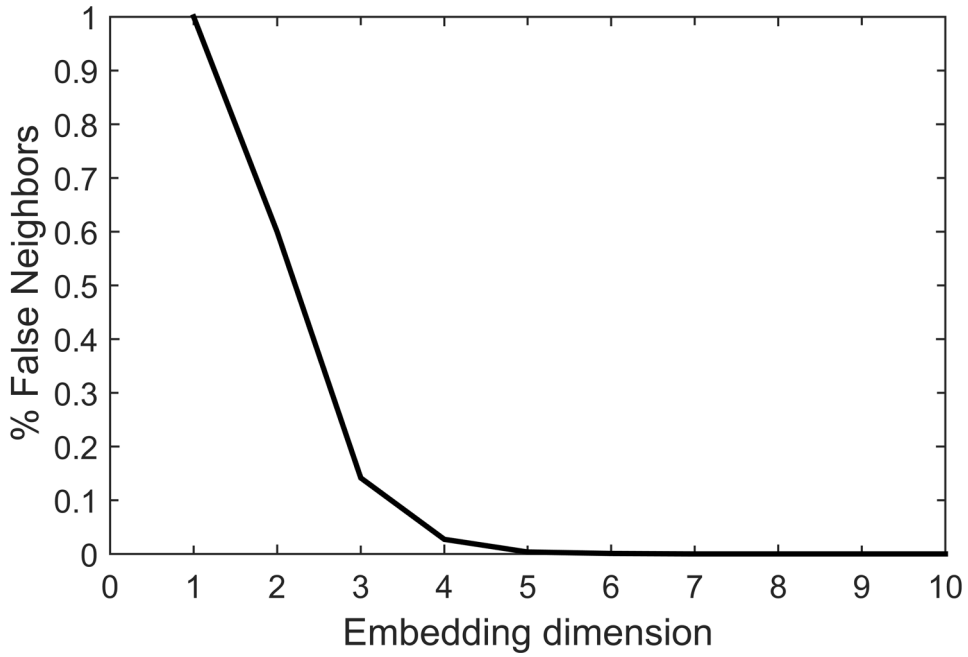

Figure 3. The percentage of false nearest neighbors depending on the choice of different embedding dimensions for a sample time-series from kinematic data.

State space reconstruction can be used to transform a single time series of a given dynamical system and "open" its dynamics, such that the states of the system can be observed. The result of this technique is the reconstruction of the full dynamics of a complicated nonlinear system[12]. Although the reconstruction is, of course, not identical to the internal dynamics of the system, it allows one to explore important properties that would be otherwise not visible in the original time series. Following the reconstruction of the series there are numerous calculations or observations that one can make, such as the estimation of the maximum Lyapunov exponent.

1.1.2.2 Numerical calculation

The maximum Lyapunov exponent is a measure of the exponential rate of divergence between trajectories of the state space and quantifies the local dynamic stability of a system. There are numerous examples were maximum Lyapunov exponents have been utilized (e.g. mechanical engineering, chemistry, biology)[6,22], but have been used all the more to determine the local dynamic stability in human locomotion. The example provided in Figure 4 is a reconstruction from kinematic data acquired from gait.

Lyapunov's theory of dynamic stability indicates how the dynamics $\mathbf{x}(t)$ of a given system react to a perturbation[7]. The temporal change in the size of a perturbation is assessed as the distance:

$$d(t) = \| x(0) - x_e(0) \| \quad (3)$$

where x(0) represents the perturbed and $x_e(0)$ the unperturbed point in the reconstructed state space.

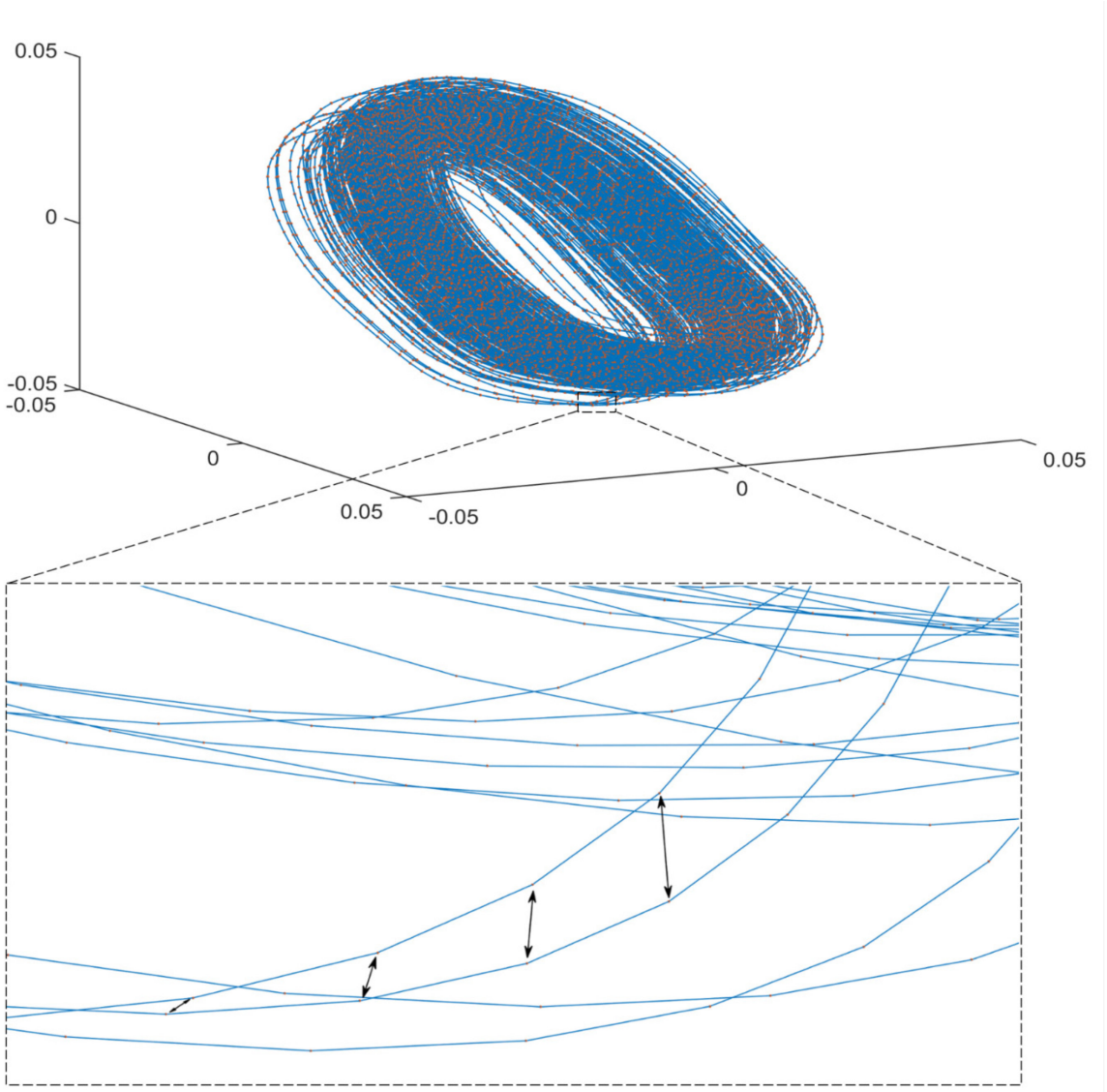

Figure 4. The reconstruction of the one dimensional time series into the state space and a magnified part of the reconstruction. The arrows denote the development of the initial separation between two neighboring trajectories.

There are three constructs according to the temporal change in d(t); ordinary stability, asymptotic stability, and exponential stability. Exponential stability is the most used stability construct and is used to provide a measure (i.e. Lyapunov exponent) to parameterize d(t). The mean growth rate of the distance between neighboring trajectories (Figure 4) in state space can be seen as:

$$\| \delta x(t) \| / \| \delta x_0 \| \quad (4)$$

The solution to the above formula can be given by the maximum Lyapunov exponent, which can be estimated for a time t as:

$$\lambda = \lim_{n \to \infty} \lim_{\delta x(0) \to 0} \frac{1}{t} ln \frac{\|\delta x(t)\|}{\|\delta x(0)\|} \quad (5)$$

Computationally, the exponent λ is estimated after the average divergence of each point's trajectory to its closest neighbor has been calculated. Specifically, the λ is estimated by the slope of the linear fit in the resulting average divergence curve. The number of data points chosen as the fitting region in gait studies is usually equal to one step (Figure 5).

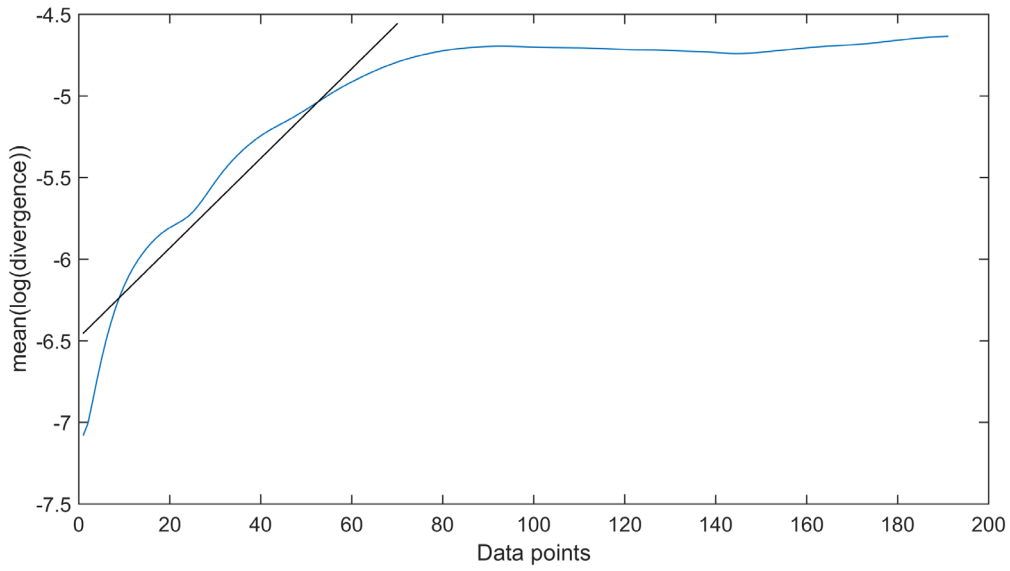

Figure 5. Resulting divergence curve of the mean logarithmic expansion of all neighboring trajectories and linear fit on the first part of the curve. The slope of the fit corresponds to the maximum Lyapunov exponent.

1.1.2.3 Properties

The most striking feature of chaos is the unpredictability of the future despite a deterministic time evolution[22]. The calculation of Lyapunov exponents has been one of the most popular methods used to detect the presence of chaos, which constitutes a nonlinear property of dynamical systems.

The most common properties of the maximum Lyapunov exponent are as follows[6,22,8]:

1. The resulting maximum Lyapunov exponents are independent of both the metric used to determine the distance between perturbations and the choice of variables. This property implies they are dynamical invariants and thereby provide an objective characterization of the corresponding dynamics.
2. A strictly positive maximum Lyapunov exponent is often considered as a definition of deterministic chaos (when the corresponding unstable manifold folds back remaining confined within a bounded domain). Moreover, it is synonymous to exponential instability (with a few exceptions such as the so-called Perron effect).
3. An inability of the system in examination to diminish the perturbations results in a higher divergence of the trajectories in the state space and thus greater value of the maximum Lyapunov exponent. Hence, the higher value of the maximum Lyapunov exponent, the lower the stability of the system.
4. Larger exponents are indicative of a greater sensitivity to local perturbations.

1.2 Dynamic stability during locomotion

> *"I would urge that people be introduced to chaos early in their mathematical education. Chaos can be studied phenomenologically by iterating it on a calculator, or even by hand […] Not only in research, but also in the everyday world of politics and economics, we would all be better off if more people realised that simple nonlinear systems do not necessarily possess simple dynamical properties."*

Robert May, 1976 [23]

Stability of human upright weight-bearing posture is achieved, provided the vertical projection of the center of mass falls within the base of support. However, locomotion is challenging this notion, since the base of support and the center of mass are in constant motion and the base of support is constantly changing its size, providing the grounds for a dynamic equilibrium state[24]. Indeed is has been often proposed that cortical areas processing the spatial, temporal and other cognitions needed to achieve vertical balance, was an important reason for brain size expansion of *Homo erectus*[24,25]. In human locomotion, the muscles and joints across the upper and lower body must coordinate to successfully perform a cyclic task. To maintain functional locomotion, the nervous system must confront the classic "degrees of freedom" problem in motor control as this was posed by Bernstein[26]. The problem arises from the vast redundancy (i.e. that multiple ways exist to execute a specific task) in the musculoskeletal system. The immense amount of degrees of freedom at the actuation or execution level of the human system is generally accepted to pose a problem to the nervous system, since the task requirements are not sufficient to uniquely specify how each muscle and joint must be controlled[27,28]. This redundancy requires a large number of elements to be coordinated in achieving the required task, while on the same time to select one possible solution amongst many[27]. However, it may be necessary to allow flexibility in motor tasks such as posture, balance and stability control, due to the adaptability of the neural systems and the requirements to perform parallel tasks[27–29].

In this section different measures of dynamic stability during human locomotion will be shortly presented and categorized. How dynamic stability changes under specific conditions,

after pathology or between age groups will be discussed next. Following, methodological considerations that influence the calculations and resulting exponents will be presented.

1.2.1 Measures of dynamic stability during locomotion

Stability in dynamic conditions such as locomotion, is crucial to uninterrupted task execution and requires effective regulation by the CNS[4,30,24,27,31]. Most commonly stability is defined as the ability to maintain the system's original state despite the influence of perturbations[7]. During functional locomotion stability is defined as the ability to maintain a locomotion pattern despite the presence of small kinematic disturbances or control errors[32,33]. Firstly, it is important to distinguish between active and passive control following perturbations in a system. For instance, active control is not always needed, since it has been demonstrated that passive dynamic walkers can recover from small perturbations, and keep walking after such perturbations without any imposed control[34,35]. Their ability to maintain locomotion has to be appropriated to the intrinsic properties of the system, such as inertia, and to the type of locomotion, which evidences that absence of any active control can still lead -to a very small extend- in effectively stable locomotion[32]. Some part of stability is, thus, attributed to the mechanical properties and the movement pattern of the system. However, the accumulation of several smaller perturbations or existence of larger perturbations require active, corrective actions from the system to maintain the movement pattern. In order to handle and overcome larger perturbation paradigms, previous studies focused on some sort of controllers[36,37], which represent an active control of the system.

Based on this knowledge, three requirements can be identified so that stable locomotion is achieved[32]:

a) The system has to be able to recover from small perturbations
b) The system has to be able to recover from larger perturbations
c) Any single perturbation encountered must be within the limits of the system (i.e. the system's ability to recover must be greater than the perturbation)

While, several measures address the above conditions independently, measuring the dynamic stability in the human system is not a trivial task. It can be that one can -in an excellent

manner- handle smaller, but not larger perturbations or one is able to recover in a single movement from a very large perturbation, but cannot handle the accumulation of consecutive smaller ones. Below the most prominent measures of dynamic stability are presented.

- Measures associated with the ability of the system to recover from small perturbations include: the local dynamic stability, the maximum Floquet multiplier, variability measures, long-range correlations, the extrapolated center of mass concept, the concept of stabilizing and destabilizing forces and the foot placement estimator.
- Measures associated with the ability of the system to recover from larger perturbations include: the gait sensitivity norm, the concept of stabilizing and destabilizing forces and the foot placement estimator.
- Measures that reflect the maximum perturbation that can be handled by the system: the maximum allowable perturbation.

Although, one can find several advantages and disadvantages in using any of the above measures in estimating the dynamic stability of the humans, recent reviews have proclaimed the local dynamic stability, estimated through the maximum Lyapunov exponent, a prominent measure among them[32,38,39].

1.2.2 Local dynamic stability under specific conditions and populations

Typically, the maximum Lyapunov exponents are estimated through kinematic data from coordinates or the derivatives thereof. A standard experimental setup is shown in Figure 6. However, in real life, such perfect conditions are not always present. It is therefore of great importance to identify how is the stability affected when different conditions are encountered during locomotion. For instance, how is the dynamic stability affected when unsteady, barefoot walking or running on a treadmill are encountered? How do age or pathology affect the dynamic stability?

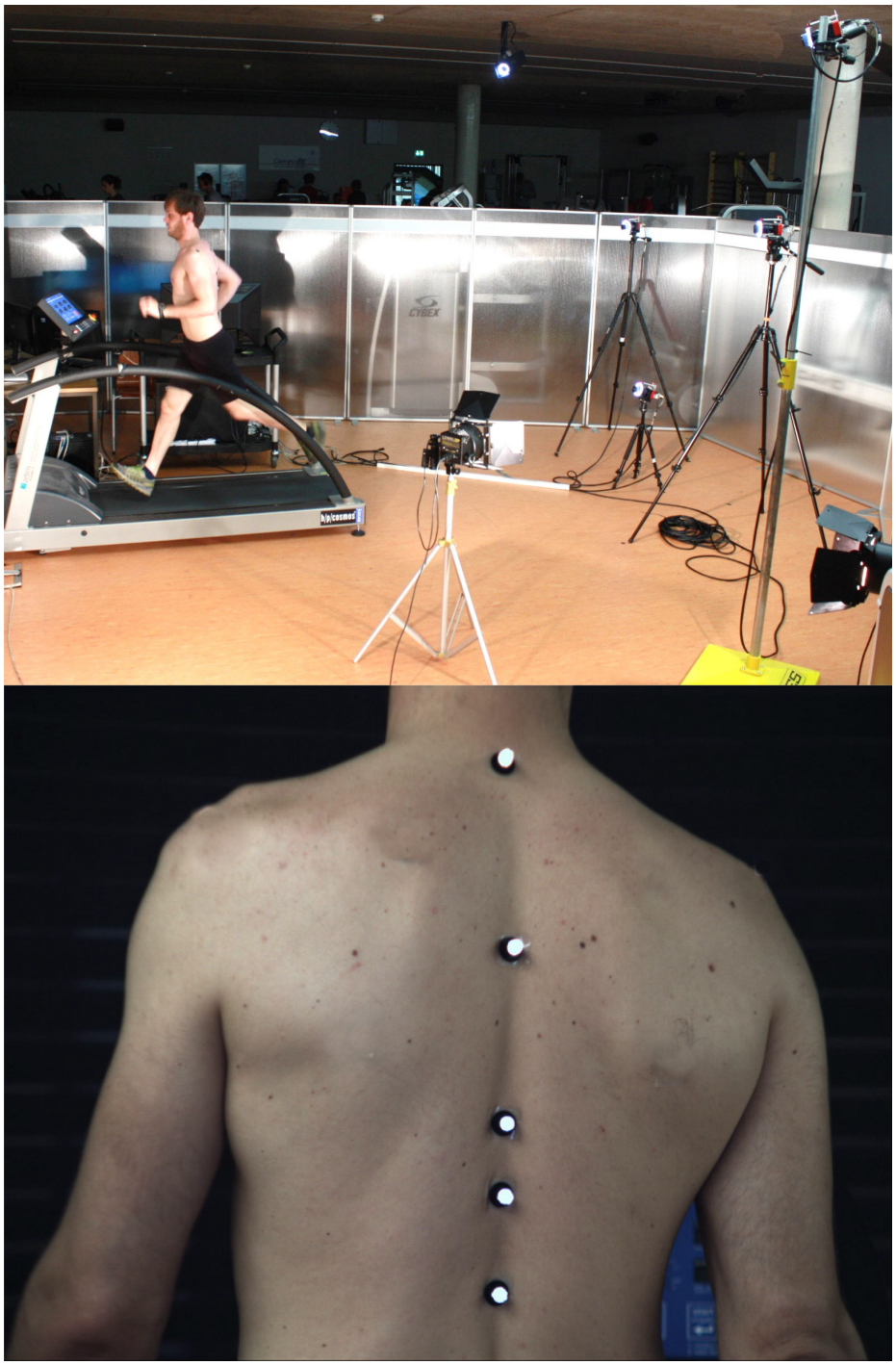

Figure 6. Typical treadmill experimental setup (top). Five cameras are capturing the kinematics of reflective markers placed on the participant's trunk (bottom). The extracted coordinates are utilized to calculate the dynamic stability of the movement using the maximum Lyapunov exponents.

In a recent paper the dynamic stability was compared between steady and unsteady locomotion using fixed speeds[40]. In both walking and running the dynamic stability was lower in the unsteady (i.e. perturbed) locomotion[40]. It seems, thus, that when stability is challenged the maximum Lyapunov exponent increases[40,41]. This increase in instability seems to be higher as the magnitude of the induced perturbations is increased[41]. Similarly, Sloot et al.[42] and Van Schooten et al.[43] reported that destabilizing subjects by means of galvanic vestibular stimulation led to increased values of maximum Lyapunov exponents. Finally, McAndrew et al.[44] reported that perturbations on the support surface or the visual scene led to gait destabilization, which was reflected in a decreased local dynamic stability.

Previous studies have also concluded that the maximum Lyapunov exponent values were significantly higher for amputees than for healthy controls, meaning that the amputees were locally less stable than the able-bodied controls[45,46]. In accordance to the previously reported effect of perturbations, both amputees and non-amputees exhibited an increased maximum Lyapunov exponent in response to the mechanical balance perturbations[45]. It also seems that the local dynamic stability decreases in a number of pathological conditions in comparison to healthy controls[47–49]. Actually, the absolute maximum Lyapunov exponent values have shown to increase 8.9% in patients with focal cerebellar lesion[49] or even 21% in patients with various neurological diseases[48].

Increased age in healthy adults is associated with extensive changes in the central nervous[50,51] and musculoskeletal systems[52–54]. Subtle age-related deficits in muscle performance have a direct impact on task execution[55], which can worsen in certain diseases due to reduced proprioceptive responsiveness[53]. Impairments in basic and complex functional tasks, such as deterioration of dynamic stability[38] is expected and has been extensively verified in adults with increased age[56,57,38,58–60,39]. In older adults the maximum Lyapunov exponent typically increases about 7.6 - 25% [56,58,61].

Falls are among the most common and serious problems that older adults are facing[62]. Approximately 30-60% of people aged 65 and over, experience unintentional falls at least once a year[63]. This percentage increases significantly with age and frailty level[63,64]. Recurrence of falls is common and very often leads to fractures, overall decrease in quality of life, hospitalization and death[63]. Epidemiological studies show that unintentional injuries

are the fifth leading cause of death in older adults (after cardiovascular disease, cancer, stroke and pulmonary disorders), while falls alone are responsible for two-thirds of these deaths[63]. Measures that estimate the stability of locomotion and predict falls are, hence, of crucial importance. Indeed, the maximum Lyapunov exponents have been found in a number of studies to be important predictor of falls, meaning that an increased value of the parameter could be associated with a higher probability of falls[65,38,32,48].

1.2.3 Methodological considerations

In the previous section it was presented how by using the Lyapunov analysis one is able to infer internal variables of locomotion and neuromuscular control in human locomotion. These results can be helpful in understanding, characterizing, and predicting the behavior of the human dynamical system[12,22]. All studies have reported a positive maximum Lyapunov exponent in gait dynamics, irrespective of the measurement device, participant group or computational methodology approach.

However, while nonlinear time-series analysis is a valuable tool in examining such invariants of a dynamical system, it is sensitive to different methodological approaches[12,22]. The absolute maximum Lyapunov exponent can be influenced by a number of decisions pertaining the calculation. For instance, the transformation –e.g. position, velocity, PCA- of the original time-series can affect the estimation[66]. Different algorithmic approaches have, also, been proposed for the estimation of the maximum Lyapunov exponent[22,67,68] and the chosen algorithm can yield different values[69–71]. Moreover, time-series acquired from signals in different positions of the human body exhibited different values for the exponent[59,72,73].

Most importantly though, it seems that the analysis can be influenced by the chosen reconstruction parameters[74,22,66,12]. In theory a valid state-space is one that uniquely defines the state of the system at all points in time[22]. Different values for delay and embedding dimension can yield very different state-space reconstructions [12,22,74]. A reconstruction of the same time series is shown in Figure 7 depicting how different numbers of delay can affect the actual reconstruction. What is more, the resulting values for the maximum Lyapunov exponents can significantly vary based on different choices of delay as depicted in Figure 8. Each of the time series used for analysis, however, represents a different dynamical system

and a different set of parameters individually optimized to the series at hand, would best describe all the states of the system[22]. Based on that notion, i.e. each dynamical system is unique, it might be optimal to implement a personalized reconstruction based on the time series deriving from the locomotion patterns of each individual.

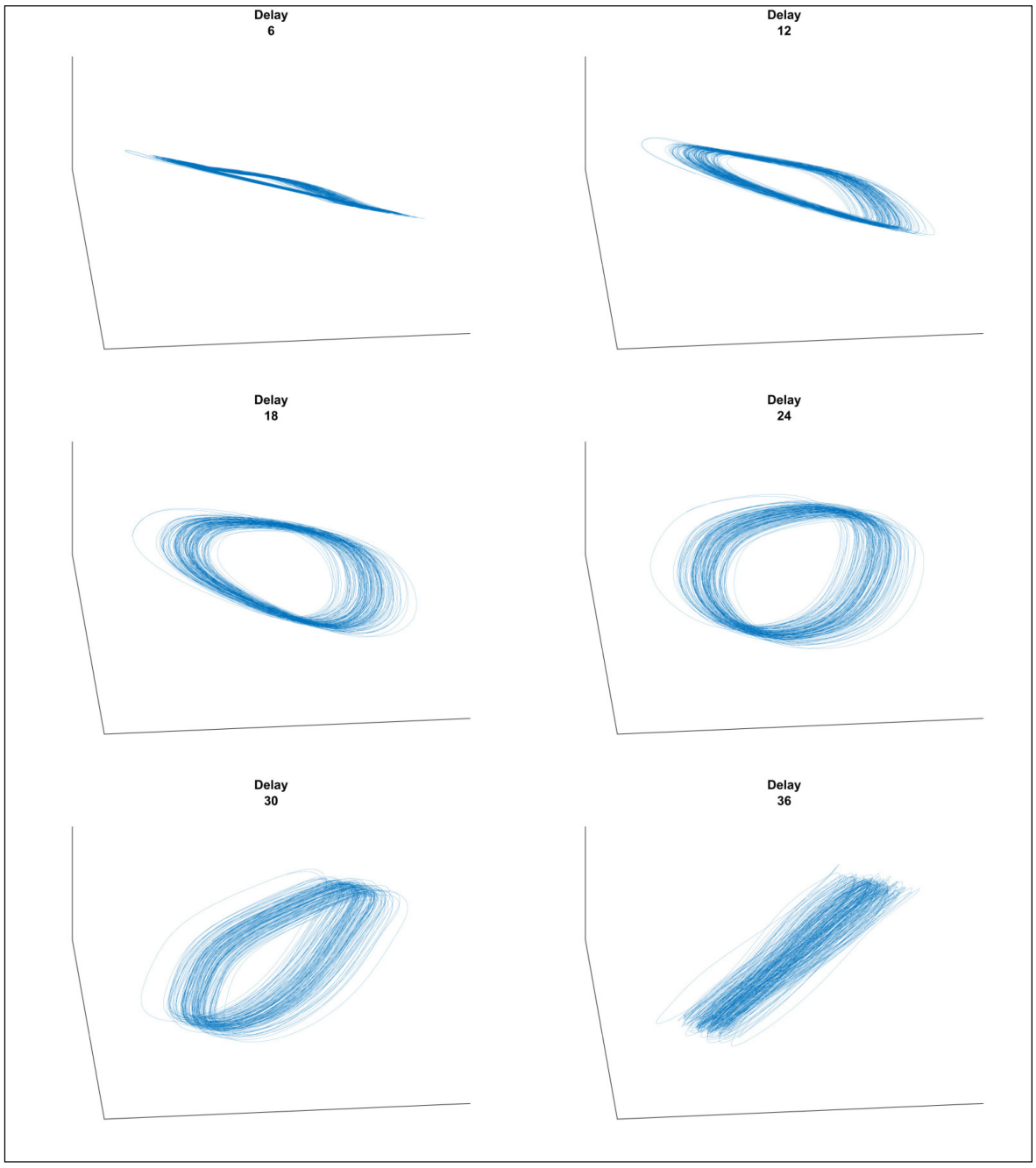

Figure 7. Three dimensional reconstruction of a sample time series given the same dimension value, but using six different delay values. For the given example the value given by the first minimum of the average mutual information function is the reconstruction based on a delay of 24.

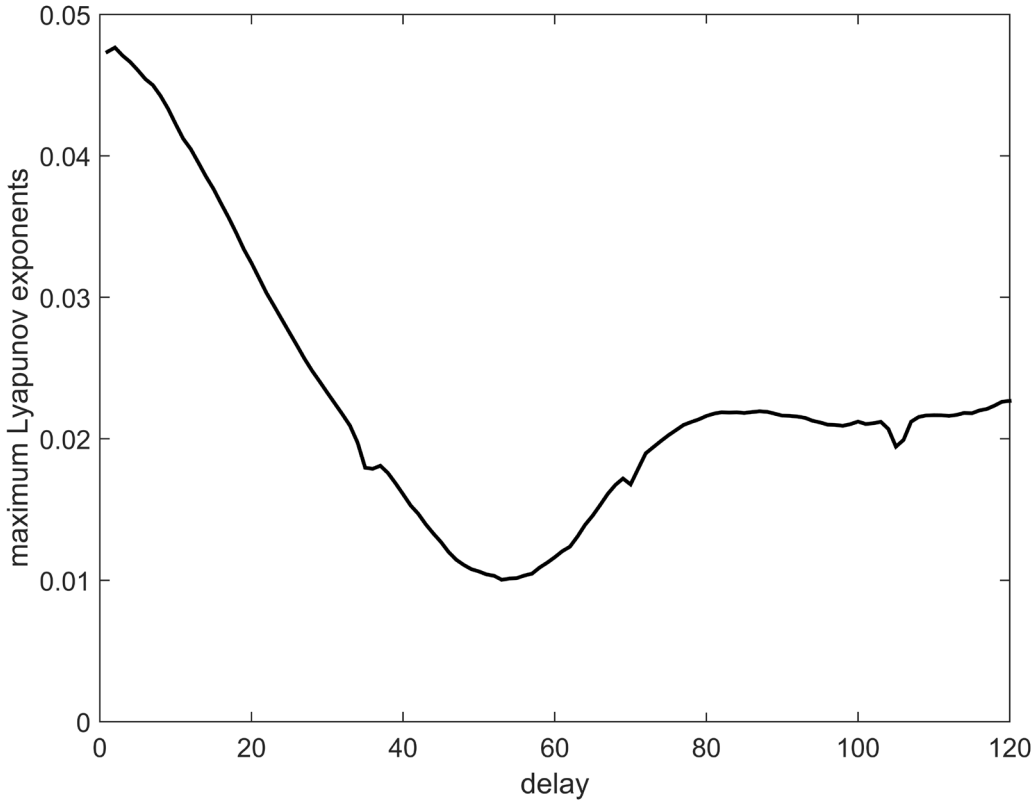

Figure 8. The figure depicts the resulting maximum Lyapunov exponent values for one sample time series in which different delay values were utilized for the state space reconstruction.

1.3 Running energetics

Energy is the currency of life. The energy cost of transport is the energy efficiency of transporting of a system (motorized or non-motorized) from one place to another. Running energetics studies the energy cost of running, a sub-category deriving from the notion of energy cost of transport applied in humans. The earliest attempts to describe the energetics of human locomotion in quantitative terms focussed on walking[75,76] and date back to 1859 till 1895[76]. The reported values at the time were surprisingly close to the ones accepted today. In the past decades there are numerous works regarding how different physiological and biomechanical factors may influence the cost of running[77–84]. In the past years, some excellent reviews summarizing the current knowledge have been written[79,81,83,84]. However, training induced alterations aiming towards improvements in the energy cost of running have only rarely and mostly recently been performed in humans.

This section will start with a historical overview regarding how "energy" appeared into the world of science and how it has taken the form in which is used today. In the same perspective how muscle energetics came to be discovered will be presented and the importance of endurance running for humans explained. What determines the energy cost of running will be introduced, upon which a discussion on how training modifications can affect it will follow.

1.3.1 Historical note

It was Aristotle (384–322 BC) that coined the term energeia, by joining εν (translates as: in/with) and έργον (translates as: work) to form ενέργεια (translates as: energeia)[85,86]. The term is closely connected to that of entelechia, and their definition most probably was used to describe "actuality" and/or "complete reality". According to Aristotle, every object's existence is maintained by energeia related to the object's function. Although initially formulated as a qualitative philosophical concept, the verb ενεργείν thusly came to signify motion, action, work and change[87]. Gottfried Leibniz proposed the Latin *vis viva* (living force) to describe a property which was defined as the product of the mass of an object and its velocity squared. This property, known to us as kinetic energy, differs from *vis viva* only

by a factor of two. It would be already 1807, before Thomas Young in a lecture at the Royal Institution uses the term "energy" instead of *vis viva*[85]. Three decades later, in 1842, the seventh edition of the Encyclopedia Britannica would eventually offer a very brief entry, describing energy as “the power, virtue, or efficacy of a thing”.

The ground work for advances in the measurement and understanding of energy began in the seventeenth century[85,86]. However, the foundations were set later during the course of the eighteenth century. The effort was aided by the adoption of both Isaac Newton’s (1642–1727) comprehensive view of physics and engineering experiments, such as those of James Watt’s (1736–1819)[86]. Moving forward, the English physicist James Prescott Joule (1818–1889) performs a large number of experiments and discovers the correct value for the equivalence of heat and mechanical energy. It was not long until the law of conservation of energy (i.e. that energy can be neither created nor destroyed) came to be the first law of thermodynamics. In 1905, a fundamental extension of the first law of thermodynamics, came from Albert Einstein (1879–1955) who concluded that mass itself is a form of energy. According to perhaps the world’s most famous equation, $E = \mathrm{mc}^2$, energy is equal to the product of mass and the square of the speed of light[86].

Around the same time the scientific community started being all the more interested in how humans and other animals utilize this “energy”. Locomotion intrinsically requires muscles to activate and contract. How muscles operate and utilize energy remained, however, a mystery for centuries. The M2 was the first myosin to be discovered in 1864 by the German scientist Willy Kühne[88]. It was already 1939 before the Russian couple Vladimir Alexandrovich Engelhardt and Militsa Nikolaevna Lyubimova discovered the property of myosin to breakdown ATP and release energy (ATPase)[89]. The *sliding filament theory* was born in 1954 by Hugh E. Huxley[90] after observations regarding how ATP dissociated actin from myosin and how it was hydrolyzed when myosin was detached from actin[91]. This led to a four-state model of the kinetics of the actin myosin interaction[91]. Prior to the *sliding filament theory*, it was commonly believed that fiber contraction was produced by the shortening of some large, rubber-like polymers. The mechanism for the sliding filament (i.e. the cross-bridge model) was formally proposed by Huxley after substantial evidence, and is variously called swinging cross-bridge model, cross-bridge theory or cross-bridge model

(Huxley preferred the name "swinging cross-bridge model", because, as he explained, "it was, after all, the 1960s"). Despite strong evidences, the *sliding filament theory* followed the course of many other revolutionary scientific ideas (e.g. *heliocentrism, evolution by natural selection)* and remained underappreciated for many years. It was already 1972 before the evidence weighted in favor of the new theory[91,92]. In that year, in the conference at Cold Spring Harbor, the field of actomyosin interactions was summarized and convinced the majority of participants that the *sliding filament theory* solves "in principle" the problem of muscle contraction[91]. While a lot of work had to follow so to better understand and prove the model, this attitude was correct in many ways.

1.3.2 Endurance running

Long distance or endurance running is peculiar in humans. Endurance running speeds of humans, range from approximately 2.3 to as much as 6.5 m/s in elite athletes[25]. These speeds are unique in endurance running among the primates[93]. For instance chimpanzees and gorillas can run, but they can only do so only for short distances[2,25]. It is thought that Austrapithecine species were also not capable to sustain endurance running[94]. Only since *Homo erectus,* specialized adaptations allowed humans to engage in long-distance endurance running[25] and it is often considered that exactly this trait set a major milestone on the development of the genus Homo[25]. In all probability capabilities in endurance running provided evolutionary advantages in hunting, scavenging and predator avoidance[25,95].

Human speeds during endurance running -adjusted to body mass- are relatively high compared even to non-primates[96]. The predicted preferred trotting speed for a quadruped with a similar to humans' mass would approximately be 2.8 m/s, while the trot–gallop transition would be 3.8 m/s[25,96]. Even compared to large mammals (110–170kg) such as ponies and horses, human endurance running speeds would still exceed the preferred trotting which is ~3.1m/s and the trot–gallop transition at ~4.4 m/s (Figure 9)[25,96]. Another criterion where humans are comparably good at endurance running is the sustainable distance. Human runners can typically run distances of 10 - 50 km in one day. Such distances are probably impossible for any other primate and compare only to those of specialized mammalian species[25]. One important characteristic of human endurance running may also be the range

of speeds that are economically available to humans. Horses, for instance, exhibit a U-shaped curve when considering the cost of transport across different velocities excluding many velocities within the aerobic range[25,96]. Humans on the other hand, exhibit a flat cost of transport in all endurance velocities[97]. However, previous studies regarding the scaling of the energetic cost of transport showed that the transport cost of human running, exceeds that of similar sized quadrupeds[98]. Adjusted for mass, the cost of transport in humans when running is about 50% higher compared to typical mammals[99].

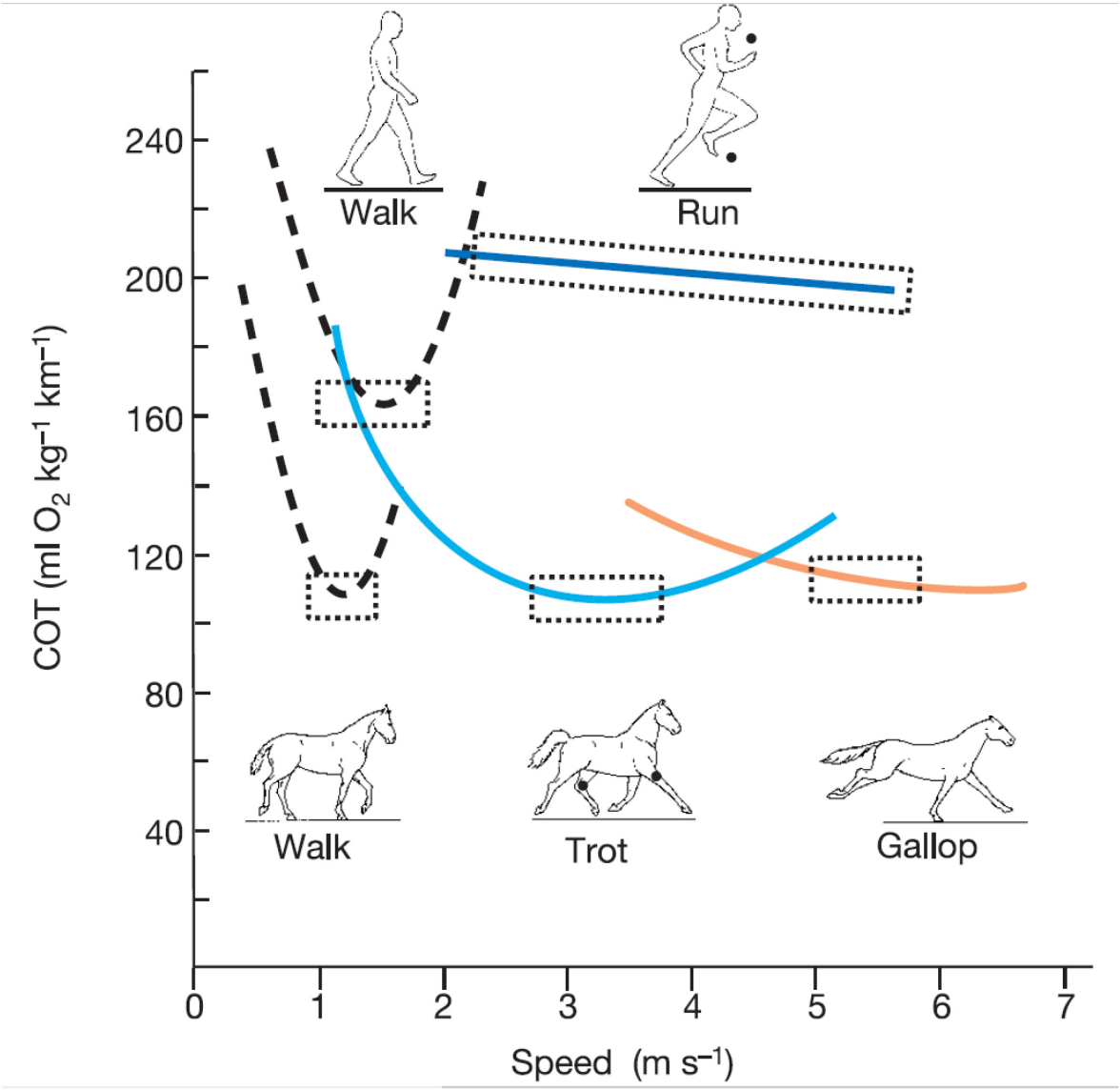

Figure 9. Comparison of the metabolic cost of transport (COT) in humans and ponies (adapted from Bramble and Lieberman 2004[25]).

1.3.3 Energy cost of running

Endurance running performance is determined by a combination of physiological, anthropometric, and biomechanical factors. It is accepted that endurance running performance depends on a complex interplay between a high maximal oxygen uptake, the ability to sustain a high percentage of VO_{2max} for long periods of time and the ability to move economically[100–102,84]. Running economy, which is defined as the rate of oxygen consumption per unit body mass (ml O_2 kg^{-1}) when running at a constant velocity[78,100] or as energy cost of running expressed as the metabolic energy cost per body weight (J kg^{-1}) and per distance traveled[75,97], has been regularly accepted to highly determine endurance running performance[103–105].

Running is, in its core, a series of muscle contractions and its energy requirements are, hence, dictated by muscle energetics. The energy cost of running is thus determined by the amount of active muscle volume and the rate at which that unit volume of muscle consumes energy[106–108]. The *in vivo* muscle energy cost arises then from the cross-bridge turnover and the energy cost of ion pumping[84,109]. Previous studies have confirmed that the rate of metabolic energy consumed in order to provide the required muscular force generation is directly proportional to the total number of cross-bridge cycles utilized by the muscles[110–112]. During running the energy cost is primarily depended on the cost of producing force in order to support the body weight[106,113,114]. On one side, the rate of metabolic energy consumption is directly proportional to the average vertical ground reaction force[108,113] and on the other, the generation of a unit of force on the ground in more expensive for a smaller than for a larger animal[113]. The amount of energy required to move a unit body weight a unit distance corresponds to W_b^{-1}, decreasing in direct proportion to body weight[99]. Hence, it can be surmised that the metabolic energy required for swinging the legs is small, since otherwise the proportionality of increased metabolic energy to increased weight would not hold[108].

In order for the system to produce forces that are similar in magnitude within a shorter time, faster muscle fibers have to be recruited, which have higher cross-bridge cycling rates and are less economical[106,111,115]. It has been, thus, supported, that small animals exhibit higher metabolic cost of running due to a greater cost associated with producing force with faster muscle fibers[106] and that the energy used by each gram of active muscle in a running animal

should be inversely proportional to the time needed to produce this force[106]. The rate of force generation can be measured through the time available to produce the force needed to support the body weight over every step, which is the time the foot is in contact with the ground[106,116,107,108].

1.3.4 Training induced alterations in the energy cost of running

Is it possible to improve the energy cost of running? There is ample evidence that well trained athletes exhibit significantly lower energy cost of running compared to lesser trained individuals[117–119]. It is thus inferred, that training protocols can directly affect and improve the energy cost of running. There are three distinct categories that can be affected with regard to how this can be achieved: muscle and tendon properties, anthropometry and running mechanics.

There is evidence that energy cost of running decreases following strength training[120,121]. Moreover, chronic endurance training could result in a higher proportion of type I (slow) fibers, subsequently positively affecting energetics in running[84]. Further, it is well established that a higher Achilles tendon stiffness and a higher strength of the plantar flexor muscles are important properties of the human system and affect the energy cost of running [122,123]. Following studies -based on these observations- proceeded with training interventions and discovered that increased the Achilles tendon stiffness and the muscle strength of the plantar flexors lead to improvements on the energy cost of running (approximately 5%)[124]. Regarding anthropometry, mass might be a trainable factor that could affect the energy cost of running[84]. Load carrying experiments by Taylor et al. (1980), showed that the energy cost of running is proportional to the exerted force during active stance[113]. Moreover, elite African runners show a lower body mass than Caucasian non-elite runners[125].

Lastly, mechanical alterations in the running strategy may provide the necessary conditions to achieve improvements in running energetics. It has been reported that alterations in stride length and stride frequency, ground contact time and foot strike patterns can have effects on the energy cost of running[79,80,82–84,126,127]. However, such mechanical alterations could be achieved not only following long-term training, but also be directly applied in maybe one or two training sessions. For experienced runners, such changes in the habitual running strategy

could be even considered to be immediately achieved. Should one expect immediate changes in the energy cost of running following acute alterations in the habitual running technique?

Following an acute mechanical alteration in the habitual running strategy, the human system must respond by initiating appropriate, but unfamiliar motor commands[24]. However, there are multiple possible combinations of muscle activations that the central nervous system has to explore and choose to achieve a given task[26,27] and timing and amplitude of muscle activity has shown a very consistent association with running economy[80]. Decreased stability has been found in face of challenging and perturbed locomotion during walking[44,41,128,40], while in surfaces where instability is expected, such as uneven surfaces, the energy cost of locomotion is increasing[129,130]. It is possible, therefore, that an unfamiliar running strategy would have an effect on the stability and the energy cost of running.

Animals and humans select among the motor control strategies in a context dependent manner based on different criteria[131,132]. As previously described, successful dynamic stability control is a prerequisite for successful execution of locomotion[24,31,133]. In some cases, studies on animals exhibited optimization of locomotion patterns to achieve increased stability, often compromising energetically optimal mechanical work output and, hence, decreasing economy[132]. It could be thus surmised that the control of locomotion is flexibly prioritized based on a context-dependent manner. The lack of appropriate learning of a new running strategy could thereof require the system to temporarily prioritize stability over economy.

1.4 Purpose of the thesis

The previous sections presented how human locomotion is a unique feature among primates and how stability being a prerequisite for successful task execution can be numerically approximated. Most importantly how the advent of new mathematical schools of thinking and advances in computing power have provided important tools to explore and understand human locomotion further, as well as, estimate critical parameters such as the dynamic stability. The current understanding of the local dynamic stability is predominantly deriving from cross-sectional comparisons of adults with and without pathology and mostly during walking. However, stability represents a universal concept in locomotion and there are only a handful of studies that ever attempted to employ the Lyapunov analysis in running humans. As such there is a clear lack of knowledge on two aspects:

- how reliable is the measurement of the local dynamic stability in walking and running?
- how can the concept of local dynamic stability extend the understanding regarding mechanisms governing locomotion?

Similarly, in chapter 1.3 the concept of energetics in human locomotion and more specifically in running has been presented. Running is receiving increasing attention as a recreational sport which is suitable and accessible to almost everybody. All the more, studies regarding running and the associated energetic cost emerge in the literature. While numerous studies attempted to identify the mechanisms of running energetics, there are only a few that performed long-term exercise interventions aiming to specific adaptations in the technique of running. However, learning new movements involves a number of interacting components such as information extraction, decision making, different classes of control, motor learning and its representations[134,135]. Runners who habitually utilize one running technique could possibly exhibit errors in the task execution, most likely induced due to a new imposed technique and lack of appropriate learning. Stability might be a particularly crucial concept in this context. Hence, there is a lack of knowledge on two further aspects:

- What kind of exercise interventions can one employ to successfully affect and reduce the energetic cost of running?

- Could stability of running have a role in the energy expenditure when a novel task is executed?

The following chapters of this thesis will endeavour to shed some light in the questions above. The above topics were addressed in three working steps with distinct purposes and hypotheses:

1. The first study presents a reliability assessment of the maximum Lyapunov exponents during human locomotion using different marker-sets. This study addresses the following points:
    a. It examines the use of multiple measurement days as a way to increase the reliability of the maximum Lyapunov exponent between days.
    b. It is the only study examining the reliability during running setting the future benchmark values in the scientific literature.
    c. Provides information regarding the effect of different markers-sets in the resulting maximum Lyapunov exponent values.
    d. Examines how the reliability of the measurement changes when different marker-sets are utilized.

It was hypothesized that the maximum Lyapunov exponents would present dissimilar values within the marker-sets and a marker-set specific reliability during walking and running (i.e. different marker-sets would exhibit different reliability values). Moreover, it was hypothesized that the reliability would improve in the block design.

2. The second study examines the local dynamic stability when an acute non habitual transition to a new locomotion condition is performed. More specifically, in this study young healthy participants that were habitually shod, as well as, their stability after transitioning to barefoot running are examined.

In this study an increased instability after the transition from the shod to the barefoot running was hypothesised.

3. The last study of the current thesis included three groups of runners. The intention of the study was to:

a. Examine the effect of a transition to a new running technique (i.e. altering the point of force application from the rear towards the mid of the foot) after a short-term (two-sessions) training on the local dynamic stability and energetics of running.
b. Study the effect of a transition to a new running technique (i.e. altering the point of force application from the rear towards the mid of the foot) after a long-term (fourteen weeks) training on the local dynamic stability and energetics of running.
c. Identify mechanisms that affect the energetics of running.

From a biomechanical point of view, a shift of the point of force application during running from the rearfoot towards the fore of the foot would result in a longer moment arm of the ground reaction force at the ankle joint and in a shorter moment arm of the ground reaction force at the knee joint. Such a change would imply a smaller for the ankle but a greater for the knee joint effective mechanical advantage. Based on previous works regarding the effective mechanical advantage[136,137] and energetics of running[106–108] it was hypothesized that this shift would decrease the energy cost coefficient and lead to an improvement in the running economy. Further, the next hypothesis was that the execution of a novel running strategy could induce instabilities and negatively affect the metabolic energy consumption and these could be alleviated by the long-term intervention training.

2 First study – The maximum Lyapunov exponent during walking and running: reliability assessment of different marker-sets

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2.1 Abstract

The maximum Lyapunov exponent (MLE) has often been suggested as the prominent measure for evaluation of dynamic stability of locomotion in pathological and healthy population. Although the popularity of the MLE has increased in the last years, there is scarce information on the reliability of the method, especially during running. The purpose of the current study was, thus, to examine the reliability of the MLE during both walking and running. Sixteen participants walked and ran on a treadmill completing two measurement blocks (i.e. two trials per day for three consecutive days per block) separated by two months on average. Six different marker-sets on the trunk were analyzed. Intraday, interday and between blocks reliability was assessed using the intraclass correlation coefficient (ICC) and the root mean square difference (RMSD). The MLE was on average significantly higher ($p<0.001$) in running (1.836 ± 0.080) compared to walking (1.386 ± 0.207). All marker-sets showed excellent ICCs (>0.90) during walking and mostly good ICCs (>0.75) during running. The RMSD ranged from 0.023 to 0.047 for walking and from 0.018 to 0.050 for running. The reliability was better when comparing MLE values between blocks (ICCs: 0.965-0.991 and 0.768-0.961; RMSD: 0.023-0.034 and 0.018-0.027 for walking and running

respectively), and worse when considering trials of the same day (ICCs: 0.946-0.980 and 0.739-0.844; RMSD: 0.042-0.047 and 0.045-0.050 for walking and running respectively). Further, different marker-sets affect the reliability of the MLE in both walking and running. Our findings provide evidence that the assessment of dynamic stability using the MLE is reliable in both walking and running. More trials spread over more than one day should be considered in study designs with increased demands of accuracy independent of the locomotion condition.

2.2 Keywords

Reliability, locomotion, humans, nonlinear dynamics, local dynamic stability, methodology, Lyapunov analysis

2.3 Introduction

Stability is crucial for uninterrupted task execution in dynamic conditions such as locomotion and requires effective regulation by the CNS [4,30,24,27,31]. As such, dynamic stability during gait refers to the ability of the system to maintain functional locomotion (i.e. not leading to falls) despite the presence of kinematic disturbances or control errors [32,33]. One parameter to evaluate numerically the dynamic stability during locomotion is the maximum Lyapunov exponent (MLE) calculated using nonlinear time series analysis and has been adopted as a criterion for the occurrence of control errors [47,56,32,58]. The MLE is based on the Lyapunov's theory of dynamic stability, initially formulated to assess the sensitivity of a mechanical system to small perturbations and is often used to quantify how the patterns of gait kinematics change in response to small perturbations [7,11]. While arguments can be made for any of the deriving stability measures, recent reviews suggested the use of the MLE as a prominent measure of dynamic stability [32,38,39] and has thus received extensive focus in the recent years[138–143,39,144,145].

Although the popularity of the MLE has increased in the context of movement science, there is scarce information on the reliability of the method, especially when comparing

measurements performed in a pre-post design after specific therapy or exercise interventions. Previous studies in walking conditions reported good intrasession reliability[146,147,48,148,149]. Based on this, it was argued that differences between young and older adults[56,150,60,39] as well as patients with moderate neurological gait disorders[48] where instability is expected, can be discovered. However, the reliability of the MLE is decreased between days[147,148]. In clinical settings where the evaluation of therapies in a pre-post design is required, the reduced between days reliability provides limitations for the detection of therapy-related alterations. Furthermore, the proof of acute changes after learning or short time adaptation (as for example while walking in different environments), needs a high degree of accuracy[41]. Based on the reported reliability between days[147,148], detection of differences after exercise or therapy-induced adaptations might not be feasible. Using a block of measurements within several consecutive days to define a representative value of the MLE might increase the reliability, thus improving the detection ability for small alterations in the MLE. To date there is no information regarding the reliability of the MLE if more measurement days are included in the calculation. Beyond walking, recently several studies investigated the dynamic stability of running using the MLE[37–40]. However, there is no available information regarding intraday or between days reliability of the MLE during running.

Nonlinear time series analysis is a valuable tool for examining the invariants of a dynamical system, but is sensitive to different methodological approaches[12,22]. To date, no consensus exists regarding the data acquisition strategies for the calculation of the MLE. While the computational aspects of the MLE calculation have been frequently examined[151,12,144,152], there is no comprehensive study examining the placement and clustering regarding data acquisition strategies. Neuromuscular control of the superior segment (trunk) is believed to enable humans maintain stability[153] and trunk control to be prioritized over inferior segments[154]. As such, while the trunk is suggested to be representative of the stability of the human system[46,155], previous studies examining the MLE employed diverse placements and quantities of markers or accelerometers. For instance, the sternum[60], the first[156] and sixth[43,157] thoracic vertebrae, the second[158] and fifth[159,147] lumbar vertebrae have been used, while clusters of two[160] or six markers[146,150,161] have also been employed for acquiring of data and subsequent analysis of dynamic stability. However, through time series analysis we compute a few characteristic numbers from a large sample of data[12,22], and data collected from

different parts of the system can contain different information regarding its states. Possible disparities in the resulting MLE deriving from different bony landmarks, could influence the results of cross-sectional, interventional or prospective study designs and comparisons across different studies that employ the MLE. Moreover, different information regarding the states of the system during locomotion across the different bony landmark positions could have an effect on the resulting reliability. It can be argued that some specific marker sets on the trunk may provide higher reliability than others, representing in a more useful way the dynamic states of the human body during walking and running.

The purpose of the current study was thus to examine the reliability of the MLE both during walking and running using six different marker-sets fixed on the trunk. Further, we aimed to investigate the effects of the different marker-sets on the MLE values. In doing so, we included comparisons of trials performed within the same day, across different days and between block measurements (i.e. three consecutive days of measurement) separated by a long period of time (in average two months). We hypothesized dissimilar MLE values within the marker-sets and a marker-set specific reliability during walking and running (i.e. different marker-sets would exhibit different reliability values) and that the reliability would improve in the block design.

2.4 Methods

2.4.1 Experimental protocol

For the current study we recruited sixteen young and healthy adults (five female), which were informed of the study's procedures. Anthropometric data of the participants were as follows: 27 ± 5 years of age; 179 ± 9 cm of height; 72 ± 12 kg of body mass. None of the participants had any musculoskeletal or neuromuscular impairments at the time of the measurements or six months prior to them. This study was reviewed and approved by the Ethics Committee of the Humboldt-Universität zu Berlin. All the participants gave written informed consent for the experimental procedure, in accordance with the Declaration of Helsinki. The participants came to the lab on six different days in total. Measurements were conducted in two blocks of three consecutive measurement days. The time between blocks

was two months on average. Each day participants executed randomly (based on computer-generated random numbers) two walking and two running trials at their preferred velocity, separated by a short resting period (60 s). In total, the participants performed twelve walking and twelve running trials per measurement block. The schematic representation of the protocol is depicted in Figure 10. A 40-60 s familiarization time preceded each trial. We recorded 270 s for each walking trial and 120 s for each running trial to ensure that a high amount of steps is included in our analysis.

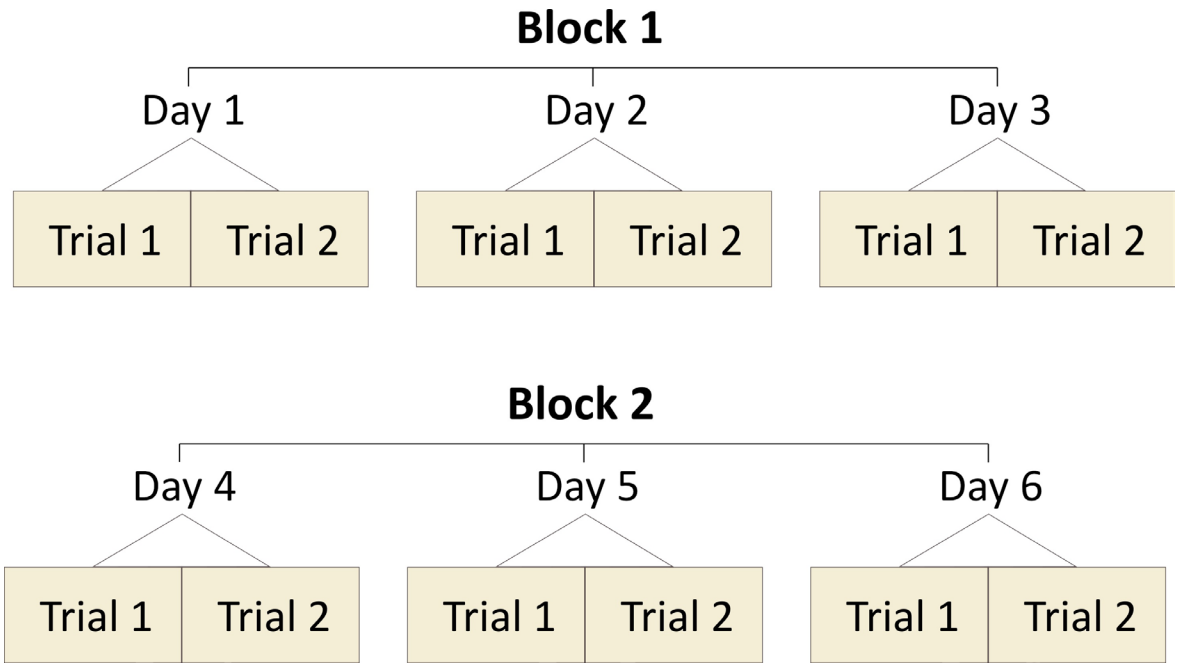

Figure 10. Schematic representation of the measurement design. All participants completed two blocks of measurements. Every block included three consecutive days of measurements (two trials per day). The design was the same in walking and running.

The individuals' preferred velocity was determined while walking and running, through the "method of limits"[162]. Following a self-selected warm-up, an experienced researcher manipulated the velocity (starting at 0.8 m/s) with varying increments of 0.05 to 0.08 m/s every five to ten seconds. The participant would then affirm when his/her comfort walking velocity was reached and the whole procedure would repeat starting from a higher velocity than the selected. The researcher used similar decrements and the participant once again affirmed his/her preferred pace. The whole process was performed at least two times and

until the selected values did not differ more than 10%. The same procedure was followed to determine the preferred running velocity (starting at 1.9 m/s).

2.4.2 Maximum Lyapunov exponents

Kinematic data were recorded through the use of five high-speed video cameras (Flare 4M180-CCL, IO Industries Inc., Canada) operating at 80 Hz during the walking trials and at 190 Hz during the running trials. We recorded eleven reflective 10 mm-markers positioned on bony landmarks of the trunk. Markers were positioned on the spine at the first (T1), sixth (T6), tenth (T10) and twelfth (T12) thoracic and the second lumbar vertebrae (L2). Further, the scapulae were recorded bilaterally on the acromia, superior and inferior angles (Figure 11). The video tracking was performed using dedicated software (Simi Motion 9.0.4, Simi Reality Motion Systems GmbH, Germany). All participants walked and ran on a treadmill (mercury, H-p-cosmos Sports & Medical GmbH, Nussdorf, Germany) with an integrated pressure plate (FDM-THM-S, Zebris Medical GmbH, Germany). A fourth order Butterworth 20 Hz low-pass filter was applied to the registered coordinates, maintaining the maximum dynamics of the system[163]. The coordinates of the markers on the T1, T6, T10 and L2 were analyzed separately. Except the time series originating from the individual markers, two clustered marker-sets were created by averaging the coordinates of several markers together on each time frame. The coordinates of all eleven captured markers formed the first clustered marker-set (ALL), while the second marker-set (SP) included only the spine markers (T1, T6, T10, T12, L2) which were clustered together as one.

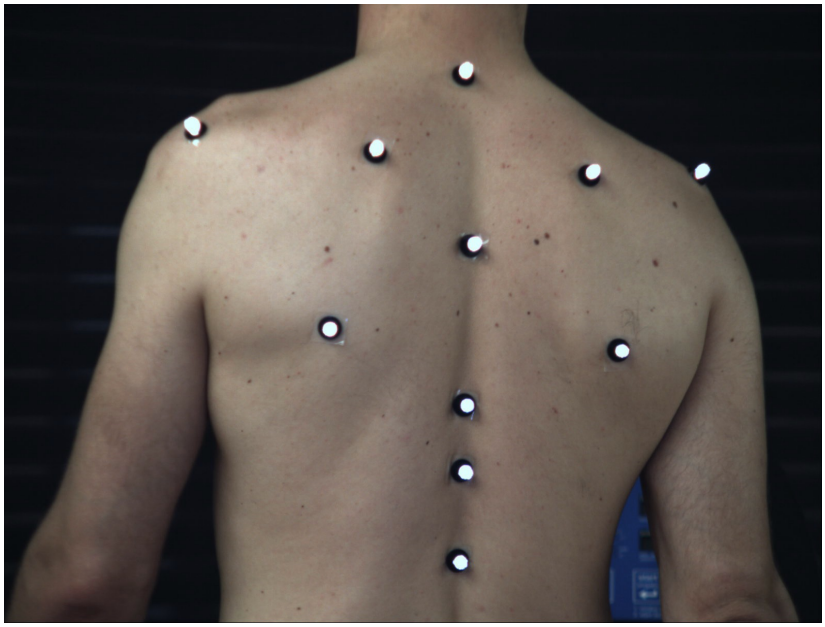

Figure 11. Marker placement on the participants' trunk. Spine: 1st, 6th, 10th, 12th thoracic vertebrae and 2nd lumbar vertebrae. Scapulae: acromion, superior and inferior angle.

We calculated the maximum Lyapunov exponents (MLE) on the vertical axis of the six time series, namely the 'T1', 'T6', 'T10', 'L2', 'ALL', 'SP'. We analyzed the coordinate data according to the procedure followed in a previous study[164]. In short, we identified the maximum common steps of all participants in all 192 trials (sixteen participants, twelve trials each) and extracted the data segment corresponding to this amount of steps in each trial. For the walking trials 454 steps were identified in all participants, while in running 279 steps were identified. This segment was then normalized to a uniform data length (based on the recorded steps and the average data points per step). For walking, the data segment consisted of 18614 data points, and for running of 19809 data points.

We reconstructed the state space from the one dimensional time series through delay-coordinate embedding[13] as follows:

$$S(t) = [z(t), z(t+\tau), \dots, z(t+(m-1)\tau)], \quad (1)$$

with S(t) being the *m*-dimensional reconstructed state vector, z(t) the input 1D coordinate series, τ the time delay and *m* the embedding dimension. Time delays were selected based on the first minimum of the Average Mutual Information function[18] and number of

embedding dimension through a Global False Nearest Neighbors analysis[21]. Individually selected time delays were chosen by averaging the outcome delays of all individual time series for each of the participants[164]. For our data, m=3 was sufficient for all participants in both walking and running, while τ ranged from 12 to 16 in walking (~0.34 of average step) and from 21 to 27 frames (~0.34 of average step) in running. We then calculated the average divergence of each point's trajectory to its closest neighbor, using the Rosenstein algorithm[68]. The MLE was calculated from the slopes of the resulting average divergence curves' linear fits. The number of data points chosen as the fitting region were equal to one step.

2.4.3 Statistics

First we performed a repeated measures two-way ANOVA to examine differences in the MLE between the different marker-sets, with trials and marker-sets as within subject factors. If appropriate, post-hoc comparisons were made with the Bonferroni correction (adjusted p-value for number of comparisons equal to 15) to determine where the effects would be present. Further, a repeated measures three-way ANOVA was employed on the MLE values to test the effect within each day, between days and between blocks separately for the different marker-sets (SPSS v.22, International Business Machines Corp., USA). We used the intraclass correlation coefficient (ICC) to determine the reliability between the trials of same day, between days and between blocks. Moreover, to determine the magnitude of the variance in the calculated values of the MLE between the trials of each day, between trials of different days and between all the trials of block one and block two, we calculated the root mean square difference (RMSD). Differences on the absolute MLE values between walking and running were examined through a Student's paired t-test. All statistical tests and procedures were performed separately for the six marker-sets (i.e. four independent markers and two clustered sets) and separately for walking and running. The level of significance for all tests was set to $\alpha = 0.05$.

2.5 Results

Participants' preferred velocity was 1.5±0.4 m/s in walking and 10.4±1.6 m/s in running. Cadence was 116.3±6.0 steps/min in walking and 160.4±8.7 steps/min in running. The values of the MLE, averaged over all trials, were significantly higher ($p<0.001$) in running (1.836 ± 0.080) compared to walking (1.386 ± 0.207) in all examined marker-sets, and thus, exhibited that running was locally more unstable than walking.

2.5.1 Walking reliability

After the first test on the effect of the marker-sets on the resulting MLE values, we found a statistically significant ($p<0.001$) effect of the marker-sets. The post-hoc comparisons showed significantly higher MLE values on the marker-set 'T6' compared to both 'L2' ($p=0.013$) and 'ALL' ($p=0.021$). Moreover, 'T10' exhibited significantly higher ($p=0.035$) MLE values compared to 'L2' (Figure 12). For the walking condition, detailed values for the results of the ANOVA, the ICCs and the RMSD of all marker-sets are presented in Table 2. No significant ($p>0.05$) differences were observed in the MLE in any marker-set when comparing trials of the same day, between consequent days or between blocks. The ICCs for all 6 marker-sets between trials of the same day ranged from 0.946 to 0.980. Between days we observed values of the ICCs ranging from 0.971 to 0.985, while the values of the ICCs between blocks ranged from 0.965 to 0.991. The RMSD exhibited values ranging from 0.042 to 0.047 when considering values of trials within the same days. RMSD values for the between days comparisons (i.e. averaged values of the trials performed in each day) ranged from 0.034 to 0.039. A decrease in the RMSD values was exhibited when considering block values. RMSD values between blocks ranged from 0.023 to 0.034. Although the reliability values were quite high in all marker-sets based on the ICC and RMSD values the marker-set 'ALL' exhibited the highest ICC and lowest RMSD within days, between days and between blocks followed by the marker-sets 'L2' and 'SP'. Both ICCs and RMSDs showed superior values between blocks in all marker-sets compared to the within and between days conditions (Table 2). A similar trend was observed when examining the divergence curves of individual participants for all trials, averaged over days and averaged per block (Figure 13).

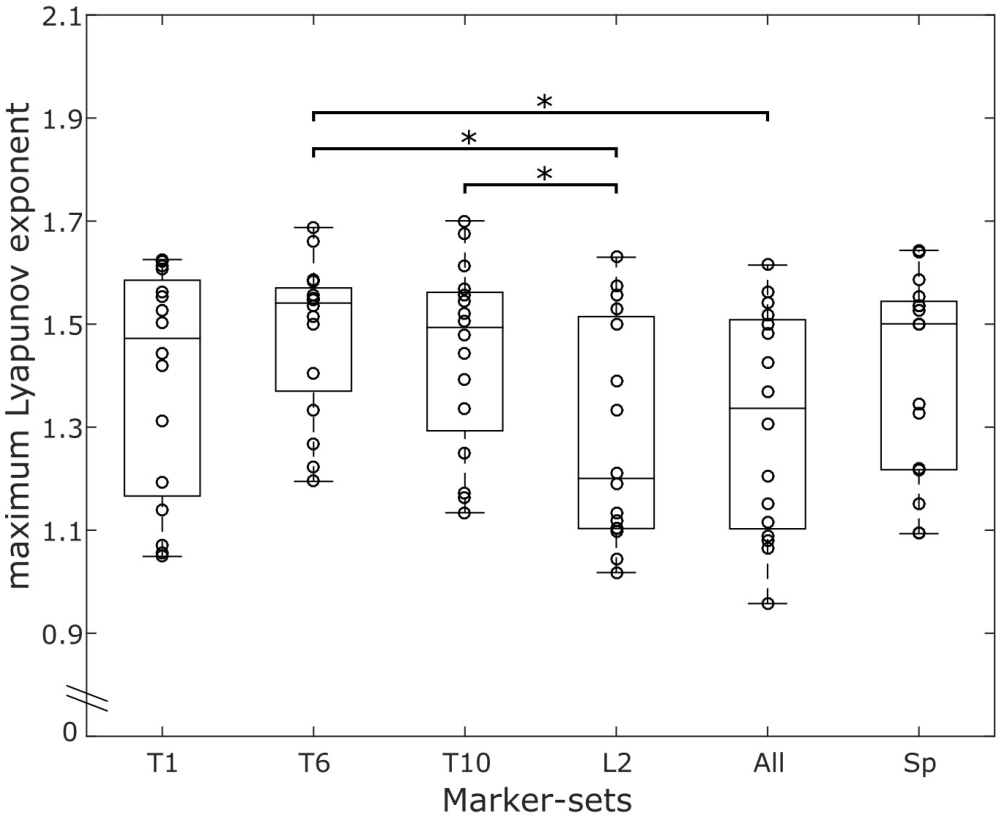

Figure 12. Overlaying graphs of boxplots and scatterplots depicting the maximum Lyapunov exponent (MLE) values in all marker-sets, during walking. Circles exhibit the individual values of the participants.

***: Statistically significant effect of marker position on the resulting MLE values ($p<0.05$)**

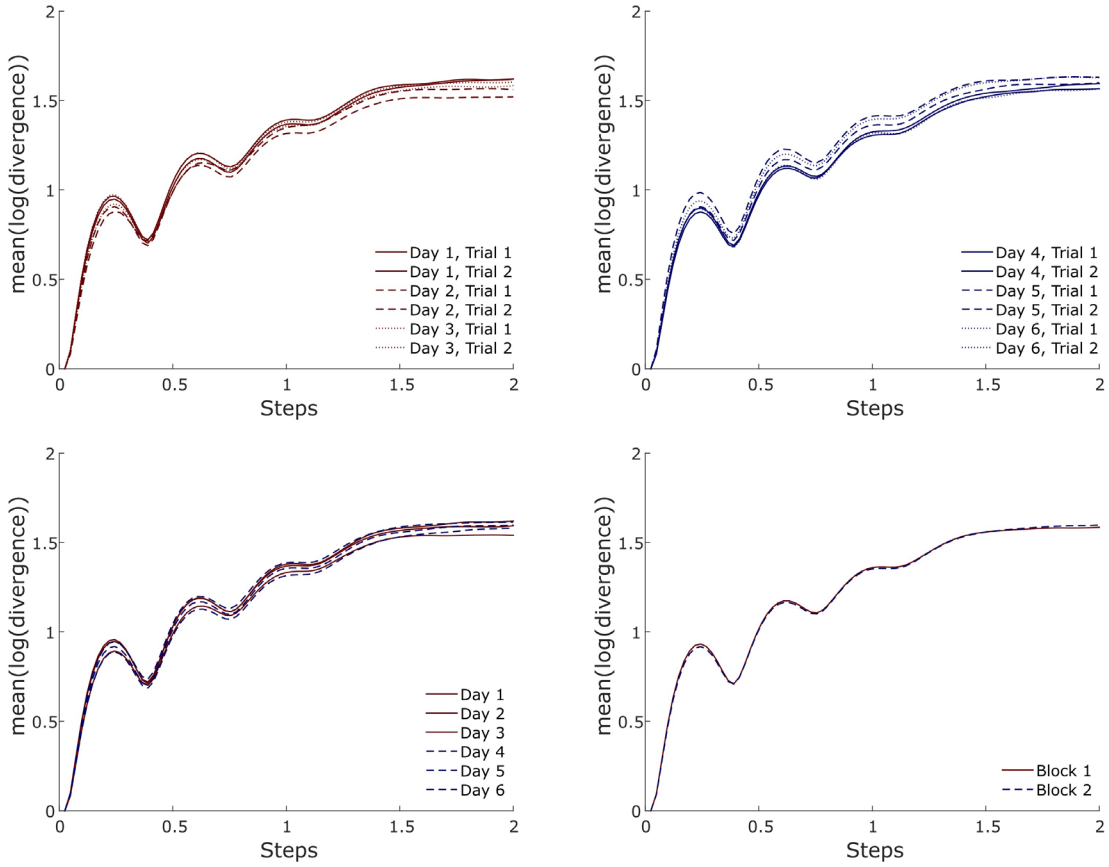

Figure 13. Exemplary (i.e. one participant and one marker-set) divergence curves for all trials, averaged over days and averaged per block during walking.

2.5.2 Running reliability

The effect of the marker-sets on the MLE values, was statistically significant ($p<0.041$). The post-hoc comparisons revealed significantly higher MLE values of the marker-set 'T6' when compared to the marker-set 'L2' ($p=0.030$) (Figure 14). Similar to walking condition we separately tested each marker-set, and the within days, between days and between blocks effect on the MLE. All values for the results of the repeated measures ANOVA, the ICCs and the RMSD of all marker-sets during the running trials are presented in Table 3. We found significant ($p=0.035$) differences in the 'L2' marker-set when comparing between trials of the same day. No further significant ($p>0.05$) differences, between trials of the same day, between consequent days or between blocks were found in any other marker-set. ICCs between trials of the same day ranged from 0.739 to 0.844 for all 6 marker-sets, while between days the ICCs ranged from 0.688 to 0.870. Further, the ICC values between blocks

ranged from 0.768 to 0.961. RMSD of trials within the same days ranged from 0.045 to 0.050. The RMSD values when considering the between days comparison, ranged from 0.038 to 0.045. Similar to the walking trials a decrease in the RMSD values was found when considering the values of blocks. The RMSD values between blocks ranged from 0.018 to 0.027. During running, the marker-set 'SP' exhibited the highest ICC and lowest RMSD between days and between blocks following by the marker-sets 'L2' and 'T10'. Similar to walking both ICCs and RMSDs showed superior values between blocks in all marker-sets compared to within and between days conditions (Table 3). This was also observed when examining the divergence curves of individual participants for all trials, averaged over days and averaged per block (Figure 15).

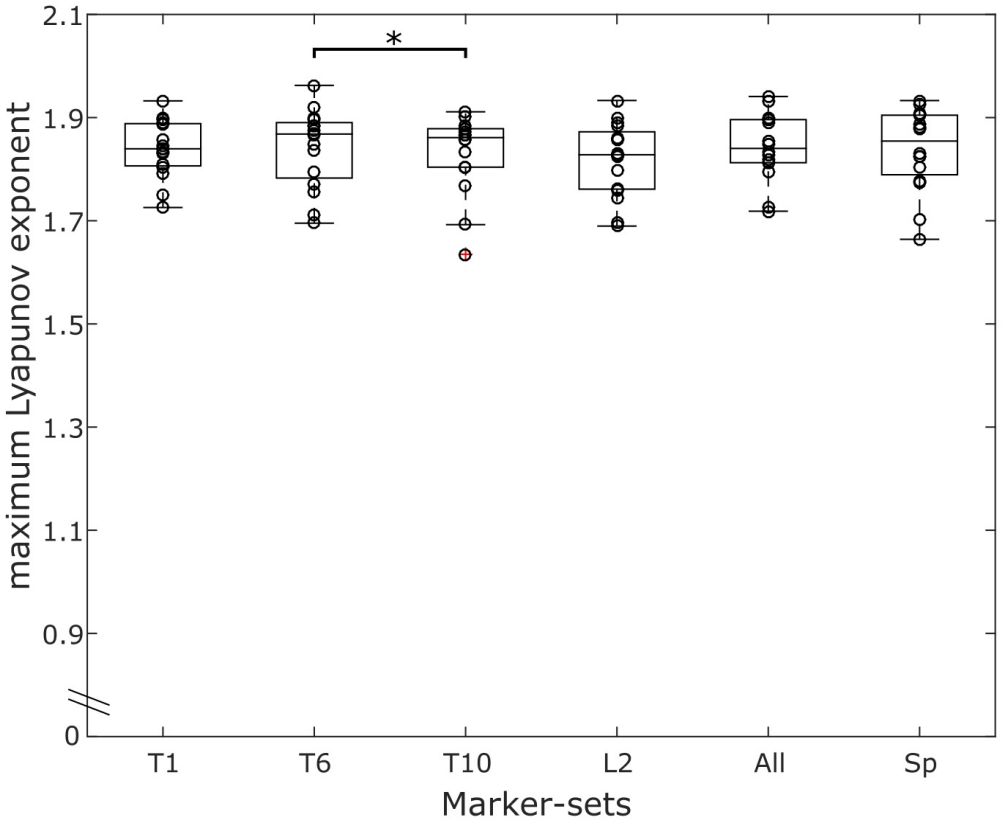

Figure 14. Overlaying graphs of boxplots and scatterplots depicting the maximum Lyapunov exponent (MLE) values in all marker-sets, during running. Circles exhibit the individual values of the participants.

***: Statistically significant effect of marker position on the resulting MLE values ($p<0.05$)**

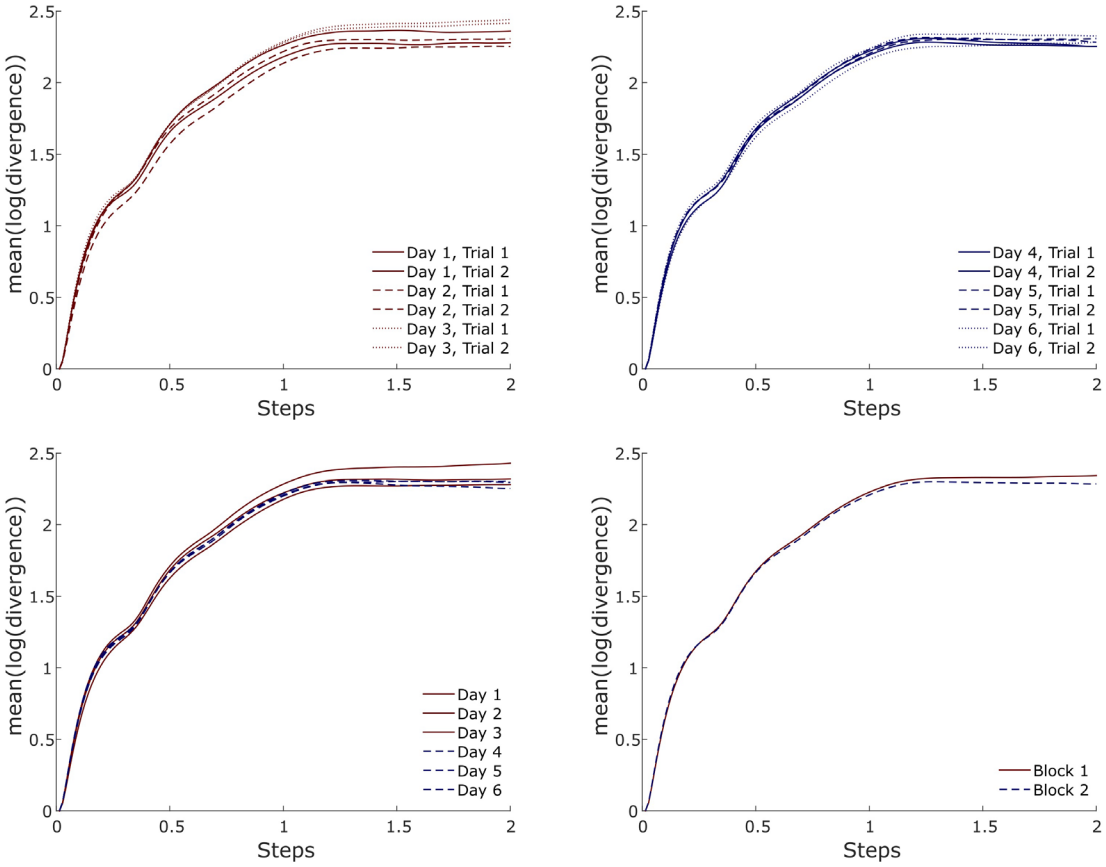

Figure 15. Exemplary (i.e. one participant and one marker-set) divergence curves for all trials, averaged over days and averaged per block during running.

Table 2. The resulting p-values and F statistic from the repeated measures ANOVA, the Intraclass Correlation Coefficient (ICC) with the corresponding upper (U) and lower (L) bounds of confidence intervals and the mean ±standard deviation Root Mean Square Differences (RMSD) for all marker-sets, when considering: both trials within the same day (within days); the averaged values of trials (between days); the averaged values of the consecutive days (between blocks). The values refer to the walking condition.

Marker-set	Within days			Between days			Between blocks		
	ANOVA	ICC	RMSD	ANOVA	ICC	RMSD	ANOVA	ICC	RMSD
T1	p= 0.579 F(1,15)= 0.322	0.978 U: 0.992 L: 0.938	0.045 ±0.012	p= 0.926 F(2,30)= 0.770	0.980 U: 0.992 L: 0.954	0.039 ±0.013	p= 0.163 F(1,15)= 2.152	0.983 U: 0.994 L: 0.953	0.033 ±0.025
T6	p= 0.978 F(1,15)= 0.001	0.946 U: 0.981 L: 0.858	0.047 ±0.018	p= 0.574 F(2,30)= 0.565	0.971 U: 0.989 L: 0.934	0.034 ±0.009	p= 0.498 F(1,15)= 0.483	0.965 U: 0.988 L: 0.905	0.034 ±0.022
T10	p= 0.911 F(1,15)= 0.013	0.966 U: 0.988 L: 0.906	0.045 ±0.018	p= 0.531 F(2,30)= 0.646	0.975 U: 0.991 L: 0.945	0.037 ±0.010	p= 0.292 F(1,15)= 1.192	0.982 U: 0.994 L: 0.951	0.029 ±0.020
L2	p= 0.686 F(1,15)= 0.170	0.979 U: 0.993 L: 0.943	0.042 ±0.013	p= 0.370 F(2,30)= 1.029	0.984 U: 0.994 L: 0.963	0.036 ±0.011	p= 0.061 F(1,15)= 4.093	0.987 U: 0.996 L: 0.958	0.027 ±0.024
ALL	p= 0.924 F(1,15)= 0.009	0.980 U: 0.993 L: 0.945	0.042 ±0.013	p= 0.244 F(2,30)= 1.477	0.985 U: 0.994 L: 0.967	0.034 ±0.012	p= 0.060 F(1,15)= 4.128	0.991 U: 0.997 L: 0.972	0.023 ±0.018
SP	p= 0.421 F(1,15)= 0.684	0.973 U: 0.993 L: 0.945	0.044 ±0.012	p= 0.879 F(2,30)= 0.129	0.982 U: 0.995 L: 0.968	0.035 ±0.010	p= 0.295 F(1,15)= 1.175	0.984 U: 0.996 L: 0.966	0.030 ±0.019

Table 3. The resulting p-values and F statistic from the repeated measures ANOVA, the Intraclass Correlation Coefficient (ICC) with the corresponding upper (U) and lower (L) bounds of confidence intervals and the mean ±standard deviation Root Mean Square Differences (RMSD) for all marker-sets, when considering: both trials within the same day (within days); the averaged values of trials (between days); the averaged values of the consecutive days (between blocks). The values refer to the running condition.

Marker-set	Within days			Between days			Between blocks		
	ANOVA	ICC	RMSD	ANOVA	ICC	RMSD	ANOVA	ICC	RMSD
T1	p= 0.516 F(1,15)= 0.442	0.739 U: 0.899 L: 0.418	0.049 ±0.014	p= 0.431 F(2,30)= 0.865	0.688 U: 0.864 L: 0.435	0.045 ±0.017	p= 0.825 F(1,15)= 0.050	0.768 U: 0.913 L: 0.449	0.027 ±0.031
T6	p= 0.055 F(1,15)= 4.319	0.844 U: 0.943 L: 0.595	0.045 ±0.012	p= 0.718 F(2,30)= 0.334	0.846 U: 0.937 L: 0.688	0.040 ±0.016	p= 0.130 F(1,15)= 2.565	0.940 U: 0.979 L: 0.835	0.023 ±0.014
T10	p= 0.116 F(1,15)= 2.782	0.822 U: 0.935 L: 0.547	0.049 ±0.013	p= 0.932 F(2,30)= 0.071	0.857 U: 0.942 L: 0.709	0.039 ±0.013	p= 0.073 F(1,15)= 3.729	0.931 U: 0.976 L: 0.802	0.024 ±0.017
L2	p= 0.035 F(1,15)= 5.341	0.819 U: 0.934 L: 0.545	0.046 ±0.015	p= 0.738 F(2,30)= 0.307	0.822 U: 0.927 L: 0.648	0.043 ±0.011	p= 0.231 F(1,15)= 1.559	0.941 U: 0.979 L: 0.842	0.021 ±0.015
ALL	p= 0.406 F(1,15)= 0.732	0.781 U: 0.918 L: 0.476	0.050 ±0.011	p= 0.423 F(2,30)= 0.886	0.794 U: 0.915 L: 0.599	0.042 ±0.011	p= 0.246 F(1,15)= 1.458	0.872 U: 0.953 L: 0.679	0.027 ±0.021
SP	p= 0.155 F(1,15)= 2.245	0.842 U: 0.943 L: 0.587	0.048 ±0.010	p= 0.952 F(2,30)= 0.049	0.870 U: 0.948 L: 0.732	0.038 ±0.014	p= 0.172 F(1,15)= 2.055	0.961 U: 0.986 L: 0.892	0.018 ±0.015

2.6 Discussion

In the present study we examined the effect of different marker-sets on the reliability of the MLE computed for each marker-set separately. The study examined these effects on different locomotion conditions, namely walking and running. All marker-sets showed excellent reliability during walking and high reliability in the running condition. The RMSD were lowest when comparing MLE values between blocks, and higher when considering trials of the same day in both walking and running. Further we found that different marker-sets have a significant effect on the MLE values in both walking and running. This effect was more pronounced while walking.

During walking, previous studies in MLE reliability have reported good (i.e. from 0.75 to 0.88)[165] intrasession[146,147,48,148,149] and moderate (i.e. from 0.53 to 0.68)[165] intersession ICC values[147,148]. The ICCs found in our study during walking were clearly higher compared to these previous studies in both intrasession (i.e. from 0.946 to 0.980) and intersession (i.e. from 0.971 to 0.985) comparisons. We recorded kinematic data for 270 s which allowed us to include a high number of steps (i.e. 454 step cycles), and reliability increases substantially as the number of recorded steps increases[146,151]. Another source of increased reliability in our study could be the use of the treadmill, in comparison to ambulatory monitoring of gait[147,166]. In walking, all marker-sets were shown to have excellent reliability and provided no significant differences when comparing within days, between days or between blocks. Measuring only one landmark of the trunk during walking could, thus, be sufficient to describe the local dynamic stability of the system and be preferred for reasons of simplification in the study design.

To our knowledge no study has examined reliability on the resulting MLE while running. During running, one marker-set (i.e. L2) showed significant differences in MLE within days and one marker-set (i.e. T1) exhibited consistently low reliability values compared to the others. The clustered marker-set ‘SP’ provided the best and more robust values in the running condition, exhibiting consistently high ICCs and low RMSD within days, across days and between blocks. The improved reliability of the clustered ‘SP’ marker-set may be attributed

to small inter-vertebrae movements that are present during locomotion[167]. The inter-vertebrae movements add another layer of complexity to the system and can affect the reliability of the MLE values. By using the clustered marker-set 'SP', these movements would possibly have minimal effects on MLE by repeated measurements due to averaging, thus improving the reliability of the marker-set. It could be suggested that, in order to achieve a high reliability in the assessment of the system's local dynamic stability during running, more than one landmark of the trunk should be considered. Moreover, the 'SP' marker-set presented no significant differences on the absolute MLE values compared to any of the other marker-sets on the trunk (Figure 12 and Figure 14), and thus, the resulting MLE values could also be representative of the dynamic stability of the system. The ICC values during running were slightly lower compared to walking in all marker-sets. While the motor programming of walking and running remains similar[168], running exhibits an increased variability and decreased regularity[169], which may explain the small decrease of the ICC values. To ensure the differences in walking and running are not dependent on the number of steps, we analyzed our walking data also including 279 steps. When matching the analyzed steps of walking to those recorded in running (i.e. when we analyzed 279 steps in walking), the results in all examined parameters for the reliability and the absolute MLE values remained in similar levels compared to when we included all 454 steps. Our findings confirmed the increased instability during running compared to walking. The higher instability during running may be due to an increased demand in recruiting and coordinating the multiple degrees of freedom faster during the task execution[72,169] affecting the assessed within days, between days and between blocks ICCs.

Although reliability was high within and between days, it increased when block measurements were introduced. This can be supported by the results of the reliability analysis with increased ICC and especially by the lower RMSD values. The divergence curves (Figure 13 and Figure 15) in both locomotion conditions further evidenced the higher reliability between the blocks. The minimum relative detectable differences (i.e. RMSD divided by the average MLE of the marker-set) were lower in the comparison between blocks. The minimum relative detectable differences results for the 'SP' marker-set are 3.1%, 2.5% and 2.1% for within days, between days and between blocks in the walking condition and 2.6%, 2.1% and 1% respectively for running. It is thus surmised that more trials spread

over more than one day can significantly improve the reliability of the measurement. To present, studies employing the Lyapunov analysis for examining the stability of gait have focused on differences between groups of young and older age[56,150,38,61,60,39] or health and pathology[170–175,49]. However, interventional or prospective study designs examining the resulting MLE might require higher degrees of accuracy and thus more than one measurement trial and day.

Based on our results, the chosen marker-set has a significant effect on the absolute value of the MLE on both walking and running conditions and that held true whether the values were obtained from a single or from clustered markers. These differences may be attributed to the nature of the theoretical concept of the used Lyapunov analysis. Time series analysis tries to identify the true dynamics regarding the states of the system from the observed time-ordered data. By measuring in a specific site or local region of the system we approximate the true dynamics, but as with any data collection we gather imperfect information. As such, different components of the system contain different parts of information regarding the states of the system and can yield altered MLE. The absolute MLE values between marker-sets differed up to 13.3% in walking and up to 1.3% in running and therefore highlight the importance of marker placement. Similar to our results, Rispens et al. reported MLE values that differed by 6.7% between two markers on the spine (i.e. when comparing the vertical component of the second and the fifth lumbar vertebrae)[73]. During walking, MLE typically increases about 8-25% in older compared to young adults[56,58,61]. Further, MLE has been reported to increase 9% in patients with focal cerebellar lesion[49] and 21% in patients with various neurological diseases compared to non-affected adults[48], while patients receiving orthopedic shoes exhibited decreased LLE by 9%[176]. These values indicate that expected differences can in some cases be affected by different marker-sets or placement errors. During running, changes of 25% have been reported in people with and without lower limb unilateral amputation[174], which would not be affected by placement differences. However, in milder cases -such as after acute transition from shod to barefoot condition with reported changes of 2%[164]- the results could be affected from different marker-sets or erroneous marker placement. This indicates that standardization in marker placement and marker-set chosen is important in study designs. Moreover, our findings exhibit the difficulty of comparing the

absolute values of MLE between studies, the results of which were obtained with different marker-sets.

2.7 Conclusions

In the current study we endeavored to examine the reliability of the MLE values using different marker-sets within days, across days and between blocks. The chosen marker-set influences the resulting MLE values. The reliability was acceptable in both walking and running for the detection of expected differences in experimental studies. However, more than one marker may be preferable to ensure high reliability in the running condition. More trials spread over more than one day, considerably improved the reliability of the MLE measurement and should be considered in study designs with increased demands of accuracy, independent of the locomotion condition.

2.8 Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

2.9 Acknowledgments

The authors are grateful to the participants for their commitment and interest during the measurements.

3 Second study – Transition from shod to barefoot alters dynamic stability during running

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3.1 Abstract

Introduction

Barefoot running recently received increased attention, with controversial results regarding its effects on injury risk and performance. Numerous studies examined the kinetic and kinematic changes between the shod and the barefoot condition. Intrinsic parameters such as the local dynamic stability could provide new insight regarding neuromuscular control when immediately transitioning from one running condition to the other. We investigated the local dynamic stability during the change from shod to barefoot running. We further measured biomechanical parameters to examine the mechanisms governing this transition.

Methods

Twenty habitually shod, young and healthy participants ran on a pressure plate-equipped treadmill and alternated between shod and barefoot running. We calculated the largest Lyapunov exponents as a measure of errors in the control of the movement. Biomechanical parameters were also collected.

Results

Local dynamic stability decreased significantly (d=0.41; 2.1%) during barefoot running indicating worse control over the movement. We measured higher cadence (d=0.35; 2.2%) and total flight time (d=0.58; 19%), lower total contact time (d=0.58; -5%), total vertical displacement (d=0.39; -4%), and vertical impulse (d=1.32; 11%) over the two minutes when running barefoot. The strike index changed significantly (d=1.29; 237%) towards the front of the foot.

Conclusions

Immediate transition from shod to the barefoot condition resulted in an increased instability and indicates a worst control over the movement. The increased instability was associated with biomechanical changes (i.e. foot strike patterns) of the participants in the barefoot condition. Possible reasons why this instability arises, might be traced in the stance phase and particularly in the push-off. The decreased stability might affect injury risk and performance.

3.2 Keywords

Lyapunov exponents, neuromuscular control, humans, running, motion analysis, nonlinear dynamics

3.3 Introduction

Nowadays, running is enjoying increasing attention on both the recreational and elite level. It was traditionally considered as a key feature of athletic shoes to support and control the foot motion during running, thus reducing shock amplification, excessive strain magnitude and rate on muscles and ligaments of the longitudinal arch[177]. Barefoot running is increasingly present in the spotlight of the scientific and commercial fields. Further, all the more runners attempt to run barefoot or in barefoot-mimicking footwear[178]. However, previous research has reported conflicting findings. It has been suggested that some of the mechanical characteristics associated with barefoot running could induce fewer

musculoskeletal injuries in runners[179], although recent studies failed to establish evidence on this argument[180]. Running economy has been shown to be a successful predictor of performance in distance running. While some studies found an improvement[181] in running economy in the barefoot condition, others were not able to identify any effects[182] and there are also studies that report a worsening[183] when barefoot compared to shod running.

Immediate transition from shod to barefoot running results in several biomechanical adjustments. Foot strike patterns change towards the fore of the foot[184], the ankle and knee joints exhibit higher and lower range of motion, respectively[185]. Cadence increases and step length decreases[185] while the arch of the foot also displays higher compression and recoil in the barefoot compared to shod condition[186]. These differences lead in altered posture and redistribution of moments in the lower extremities resulting in changes to limb stiffness, limb loading and whole body dynamics[187,188]. The central nervous system encounters variations during running, in both internal and external conditions, requiring adequate neuromuscular coordination[187]. This goal can be achieved through feedback- as well as predictive-based motor control using information about the "state" (i.e. displacement and velocity) of the system[189].

It has been often overlooked that the execution of a non-familiar task from habitually shod runners, such as barefoot running may induce novel disturbances to the system. Such a task, could initiate control errors from deficits in the perception and processing of sensory information[187,188]. In addition, errors can arise from deficits in predicting the motor commands to deal with expected perturbations[187]. There is evidence that the rate of the navicular drop[190] and the magnitude of longitudinal arch compression increased during the stance phase while running barefoot[186]. This increase indicates effects on the sensory feedback information due to intrinsic changes in the state of muscles and ligaments of the longitudinal arch. Kelly et al. (2016) reported alterations in the activation level of the flexor *digitorum brevis* and *adductor halluces* while running barefoot, which resulted in a reduction in the longitudinal arch stiffness during the stance phase compared to shod condition. We can therefore argue that control errors can be introduced during barefoot running. These could derive from deficits in the perception of the arch state and conversion of this information into appropriate motor commands as well as from the increased mechanical

demand on muscles and ligaments of the foot. Consequently, we could also expect alterations in intrinsic properties of the system such as the dynamic stability, which has never been investigated to date when comparing shod and barefoot conditions during running.

During locomotion, the local dynamic stability calculated using nonlinear time series analysis, can be adopted as a criterion for the occurrence of control errors[47,49]. The largest Lyapunov exponent (LLE), which quantifies how the system's states respond to very small perturbations -thus providing information regarding the neuromuscular control of the human system- has been often used to assess local dynamic stability during walking[47,49,171,191]. A previous study found a small effect of worsen stability in the vertical direction of movement when participants walked without shoes[192]. To date however, such approaches have only rarely been used during locomotion tasks such as running[72,174]. Alteration in the dynamic stability of the system could play a significant role when transition to the barefoot condition and constitute one mechanism contributing to the mentioned discrepancies in the literature regarding the effect of barefoot running on injury risk and performance[180,182].

The purpose of the current study was to investigate the local dynamic stability of the human system during an immediate alteration from shod to barefoot running. We anticipated that the reported intrinsic changes on the state of muscles and ligaments of the foot during the stance phase of barefoot running[186,190] would affect the demand of the neuromuscular system, initiating motor control errors. We hypothesised an increased instability after the transition from the shod to the barefoot running. In doing so, we measured several other biomechanical parameters to gain insights in the mechanisms governing this transition and examine how different parameters interact with one another.

3.4 Methods

Twenty healthy young adults (six female) were recruited to participate in the study (age 27.8±5 years; mass 72.9±11.9 kg; height 178.7±8.1 cm). None of the participants had any musculoskeletal or neuromuscular impairments at the time of the measurements and at least six months prior to it. All of them walked and ran habitually shod in their daily life. The study was conducted in accordance to the university ethical committee guidelines.

The main setup of the study consisted of five high-speed video cameras (Flare 4M180-CCL, IO Industries Inc., Canada) operating at 190 Hz to record five reflective 10 mm-markers positioned on the spine. Namely, the first, sixth, tenth and twelfth thoracic as well as the second lumbar vertebrae were recorded (Figure 16). The video tracking was performed using dedicated software (Simi Motion 9.0.4, Simi Reality Motion Systems GmbH, Germany), while raw data were post-processed using custom algorithms (Matlab 2014b, Mathworks Inc., United States). Videos were synchronised with a pressure plate (120 Hz capturing frequency; FDM-THM-S, zebris Medical GmbH, Germany) integrated in the treadmill using an analog signal triggered by the video capturing software.

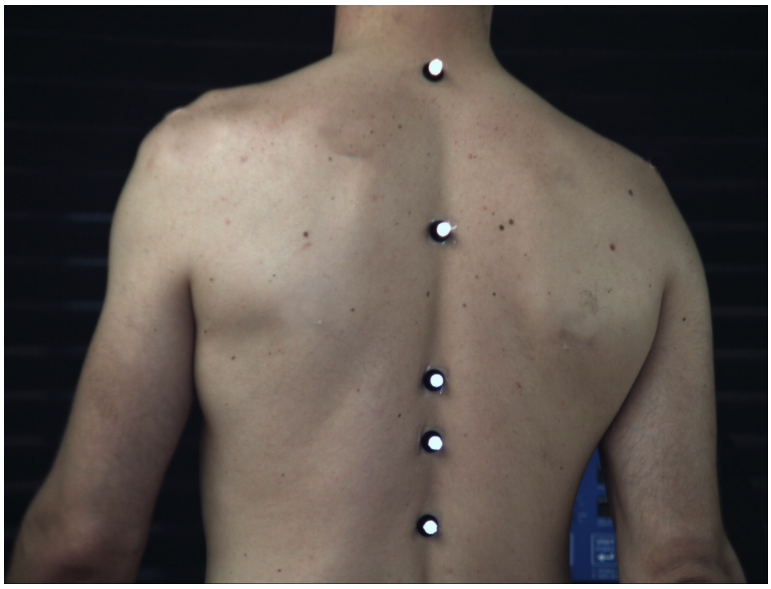

Figure 16. Marker placement on the participants' trunk: 1st, 6th, 10th, 12th thoracic vertebrae and 2nd lumbar vertebrae.

The participants executed randomly (based on computer-generated random numbers) two barefoot and two shod running trials at their preferred running speed, separated by a short resting period (60s). Each trial consisted of 40-60s familiarisation time and 120s capturing time. The individuals' preferred speed was determined while running shod, through the "method of limits"[162]. Following a self-selected warm-up, an experienced researcher manipulated the speed (starting at 1.5 m/s) with varying increments of 0.05 to 0.08 m/s every five to ten seconds. The participant would then affirm when his/her comfort speed was reached and the whole procedure would repeat starting from a higher speed than the selected.

The researcher used similar decrements and the participant once again affirmed his/her preferred pace. The whole process was performed at least two times and until the selected values did not differ more than 10%.

A fourth order Butterworth 20Hz low-pass filtering was applied to the registered coordinates. Coordinates were only lightly filtered in order to preserve the non-linear structure of the data and the dynamics of the system[47]. The vertical displacement of the trunk over the whole duration of the trial (i.e. two minutes) was calculated averaging the vertical coordinates of all investigated markers). Through the integrated pressure plate, we identified the flight and contact phase of each stepping event as well as the overall cadence. Further using the vertical ground reaction forces, we calculated the impulses (i.e. integral of the vertical ground reaction force over time) for the whole duration of the trial. The strike index (i.e. the distance from the heel to the centre of pressure at first impact relative to total foot length[193]) was calculated based on the foot pressure distribution using a validated algorithm[184]. The foot strike pattern describes how the foot touches the ground at first impact[193]. A rear foot strike pattern was considered one that provided a strike index lower than 1/3 and a mid-fore foot strike pattern one that provided values higher that 1/3 of the total foot length[193].

We calculated the LLE using the vertical coordinates of the clustered spine markers, which provided excellent stationarity. Running on a treadmill restricts the movement at the anterioposterior direction due to the participants seeking to match the speed of the treadmill. Similarly, treadmill width restricts the movement on the mediolateral direction. Previous studies revealed a dependence of the estimated LLE on the number of steps included in the calculation[151]. We, thus, identified the maximum shared number of steps (i.e. 0.5 of gait cycle) among all participants and all trials. In our experiment, the maximum shared number of steps was 278. For each time series a data segment corresponding to the coordinate data from the first until the 278th step -through their closest time instances- was extracted. This segment was then normalized to a uniform length of ~20000 data points. We captured a high number of steps while running in both conditions (barefoot and shod) to improve the reliability of the LLE's calculation[151].

State space reconstruction of the full dynamics of the system was accomplished through delay-coordinate embedding and performed from the input data of the vertical axis and time-delayed copies of each point on the time series as follows:

$$\boldsymbol{S(t)} = [z(t), z(t+\tau), \ldots, z(t+(m-1)\tau)], \quad (1)$$

with **S(t)** being the *m*-dimensional reconstructed state vector, z(t) the input 1D coordinate series, τ the time delay and *m* the embedding dimension. Time delays were calculated for each time series from the first minimum of the mutual-information curve extracted from the Average Mutual Information function and number of embedding dimension through a Global False Nearest Neighbours analysis for each time series, with a threshold of one per thousand data points.

One of the main challenges of delay-coordinate embedding is how to best represent different dynamical systems since different values of τ and m can yield very different state-space reconstructions[12,22,74]. Therefore, each series is analysed with parameters individually optimised to the series at hand[22]. Based on the notion that each dynamical system is unique, we considered every individual could be represented by a different set of parameters that would best reconstruct their data. We, thus, implemented personalised chosen parameters (τ and *m*) by averaging over all the trials performed per individual, and reconstructed state spaces accordingly. Such a strategy, being in strong accordance with nonlinear time series analysis[12,22] theory, enables reconstructions specific to the dynamical system without directly affecting the comparison between tasks. For our data, *m*=3 was sufficient for all subjects, while τ ranged from 22 to 26 frames (~0.35 of average step). The Rosenstein algorithm was employed to calculate the average exponential rate of divergence by calculating each point's trajectory divergence to the closest trajectory in the reconstructed state space. The LLEs were then estimated from the slopes of linear fits to the resulting divergence curves for 1 step (Figure 17A). The effect of condition -barefoot and shod running- was tested through paired Student's t-tests in all variables, with the significance level set at α=0.05.

3.5 Results

In the barefoot condition the LLE showed statistically significant higher values (p=0.009) compared to the shod one (Figure 17), indicating an increased instability in barefoot running. The relative changes ranged from -3% to 8.8%, with 14 out of 20 participants exhibiting an increased value of the LLE. The coefficient of variation of the LLE between the two conditions increased slightly, amounting 4.8% in the shod and 5.1% in the barefoot condition.

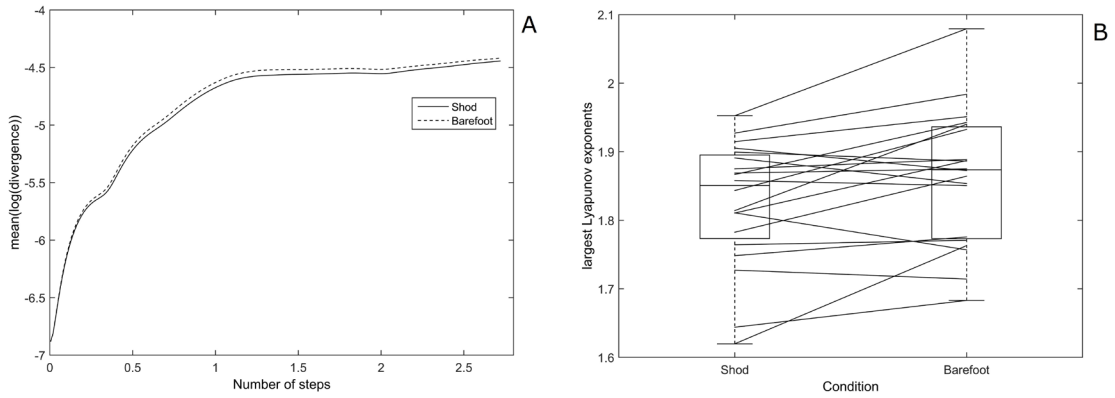

Figure 17. (A) Averaged over all participants mean logarithmic divergences between shod (solid line) and barefoot (dashed line) running. (B) Boxplot containing the largest Lyapunov exponent values for shod and barefoot running with the lines indicating individual changes between conditions.

During barefoot running, participants ran with a significantly higher cadence ($p<0.001$), increasing their step frequency by 2.2% (Table 4), while the total vertical displacement over the whole duration of the trial (i.e. two minutes) decreased significantly ($p<0.001$) (Table 4). The differences in average contact time (299±33 ms shod; 279±27 ms barefoot) and average flight time (76±28 ms shod; 89±22 ms barefoot) were both significant ($p<0.001$). The total vertical displacement over the two minutes of running was significantly lower during the stance phase ($p<0.001$), and significantly higher during the flight phase ($p=0.002$) in the barefoot condition (Table 4; data for contact and flight displacement from 14 subjects due to errors in synchronisation). In a similar manner the total contact time decreased significantly ($p<0.001$) and the total flight time increased significantly ($p<0.001$) in the barefoot compared to shod condition (Table 4). The normalized to body weight impulse decreased significantly ($p<0.001$) when running barefoot (Table 4). The strike index changed

significantly ($p<0.001$) towards the front of the foot, with 95% of the cohort rear foot striking when shod, compared to only 50% when barefoot.

Table 4. Cadence, strike index, vertical displacement of the spine over two minutes (total, during stance and during flight), total contact and total flight time over two minutes and integral of vertical ground reaction forces as a percentage of body weight per second in the shod and barefoot condition (mean ±standard deviation).

	Shod	Barefoot	d
Cadence [steps/min]	159.66± 9.27	163.11± 10.47 *	0.35
Strike index [feature scaling]	0.09±0.12	0.31±0.20*	1.29
Vertical displacement [m]	54.20± 5.36	51.98± 5.87 *	0.39
Vertical displacement during stance [m]	45.88±4.84	41.66±4.27*	0.92
Vertical displacement during flight [m]	7.29±3.76	9.30±3.23*	0.57
Contact time [s]	95.22± 9.00	90.50± 7.22 *	0.58
Flight time [s]	24.78± 9.00	29.50± 7.22 *	0.58
Impulse [BW%s]	27.40± 1.97	24.46± 2.47 *	1.32

Statistically significant differences between shod and barefoot running ($p<0.05$)
d: Cohen's Effect size

3.6 Discussion

The present study aimed to investigate the local dynamic stability of barefoot running in inexperienced barefoot runners. We, therefore, compared the LLE from 20 participants, while running on a treadmill with and without shoes. Our investigation revealed a significant lower dynamic stability in barefoot compared to shod condition indicating changes in running stability control. Further, we found a higher cadence and total flight time, a lower total contact time, total vertical displacement and impulse over the two minutes when running barefoot. The foot strike index increased towards the front of the foot.

Achieving stability during locomotion is a primary challenge for the central nervous system and depends on neuromuscular control[194]. The LLE quantifies how the system responds to small internal perturbations, revealing the ability of the system to maintain stability and detects neuromuscular control errors in achieving it[47,49]. An increased LLE corresponds to more chaotic and unstable dynamical system[12,22], thus, the increased LLE in our study provides evidence that immediate transition to the barefoot condition produced a more unstable movement pattern. It is hence inferred that the execution of a challenging locomotor task such as running barefoot without prior training, induces disturbances in the neuromuscular control. During cyclic motor tasks like running, sensory feedback information can be used to form feed-forward driven muscle activation patterns configuring adjustments of the leg at touchdown[195] to achieve a new equilibrium between sensory inputs and motor outputs. The habitually shod participants of our study when exposed to the non-familiar barefoot condition altered their running technique predominantly by moving their foot strike pattern towards the fore of the foot. Changes in the foot strike patterns need appropriate adjustments and modulations to the other biomechanical parameters[179,196]. We found a significant positive correlation (r=0.49, p=0.025) between the changes in foot strike index and the changes in the LLE from the shod to the barefoot condition (Figure 18), while there was no initial association between foot strike index and LLE. Therefore, it is possible that larger changes in foot strike patterns (i.e. running technique) could increase the system instability.

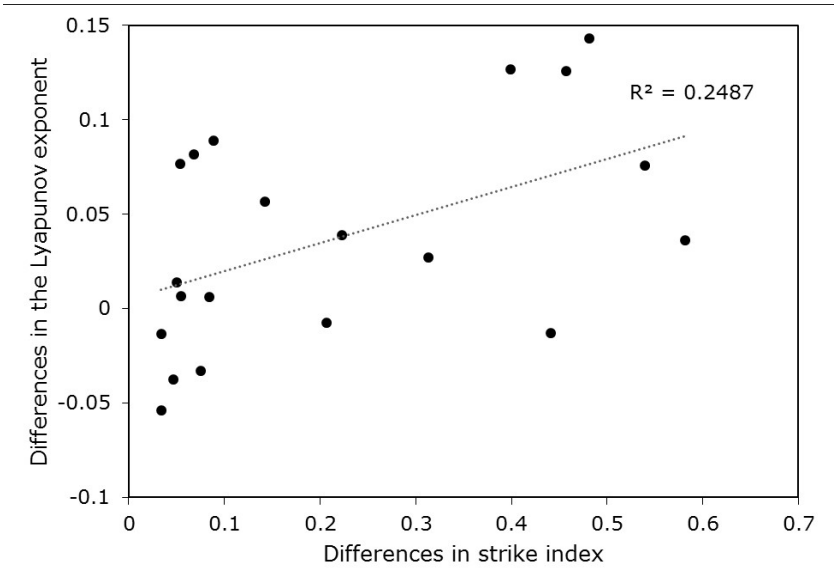

Figure 18. Changes of the largest Lyapunov exponent values and changes in the foot strike index from the shod to the barefoot condition.

During running the trajectory of the centre of mass during the flight phase is predominantly determined by the take-off conditions. Considering no external forces are applied to the human system after the take-off we can support the argument that the recognised higher instability in the barefoot running has been initiated during the time that the body is in contact with the ground. Further, we identified lower vertical displacement during the stance phase and a higher vertical displacement during the flight phase in the barefoot condition. In our study, the stance phase was 79.3% of the total time in the shod and 75.4% in the barefoot condition. Previous studies found that immediate transition from shod to barefoot running influences the moment arm of the ground reaction force at the ankle joint resulting in a lower gear ratio (i.e. the ratio between ground reaction force and muscle force moment arms) in the late stance phase[197]. Lower gear ratios at the ankle joint decrease the contact time while running[198], thus providing an explanation for the shorter average per step contact time (7%) we found in the current study during barefoot running. As such, the shortening velocity of the calf muscles may have increased, thus decreasing their force potential due to the force-velocity relationship[199]. The plantar flexor muscles are the major contributors to power generation during the late stance phase[200] and signal the appropriate timing for the flexion of the limb to initiate the swing phase[201,202]. A potential intrinsic disadvantage in their force generation and an erroneous timing in the signalling to recall the leg for the initiation of the swing phase might be a potential reason for the initiation of an instability after the immediate transition to the barefoot condition.

A recent study evidenced that after immediately transitioning to barefoot running, the longitudinal arch angle in the middle of the contact time is larger compared to shod condition[186] indicating an increased magnitude of longitudinal arch compression. A higher arch compression during the stance phase of running may increase the strain on plantar connective tissues and the mechanical demand in the longitudinal arch. Such an alteration during the change to barefoot running could constitute another possible mechanism affecting the dynamic stability. Our participants normally wore shoes during running and therefore it can be argued that the increased instability in bare foot running occurred due to the unfamiliar condition and not due to barefoot running per se. The association of the

biomechanical changes to the changes in the LLE during barefoot running indicate that larger changes in foot strike patterns (i.e. running technique) could increase the system instability. Due to the chosen experimental design, however, we are not able to clearly exclude the effects of familiarization.

Several studies found decreased local dynamic stability in a number of pathological conditions compared to healthy controls[47–49] and in the injury affected compared to the unaffected side of the same individuals[174]. The LLE has been shown to increase 8.9% in patients with focal cerebellar lesion[49] or even 21% in patients with various neurological diseases[48]. Patients receiving orthopaedic shoes exhibited decreased LLE by 9%[176] while in older adults LLE typically increases with values about 7.6 - 25%[56,58,61]. In our study the increased by 2.1% LLE indicates deficiencies in the neuromuscular control when the system was presented with the immediate change to barefoot condition. Deterioration in neuromuscular control during locomotion is associated with musculoskeletal injury and pain[80]. To date there are no clear reports in support of a definite connection between barefoot running and injury risk[180,182]. This increase might therefore indicate minor control deficiencies attributed to the altered running technique employed by our participants.

While previous studies achieved neuromuscular adaptations employing barefoot training, there are conflicting reports in the literature regarding the effect of barefoot running upon running performance[181,183]. The decreased vertical displacement during barefoot running translated into 2.2 m less movement in the total duration of 120 s and would have beneficial effects on running economy[203]. Similarly, the 11% decreased vertical net impulse on our study suggests that barefoot running resulted in less vertical motion amplitude. On the other hand, neuromuscular control is required for effective and fast locomotion and constitutes a determining factor of running performance[80]. Hence, the reduced stability during barefoot running might negatively affect running economy. Moreover, the higher cadence in barefoot condition increases the amount of activations and deactivations of the muscles in the lower extremities for a given distance and result in higher energy cost per unit distance[204]. It appears *ergo* that neuromuscular factors contribute differently and may weight in both directions of the scale, leading to conversing effects regarding the overall running economy between shod and barefoot running.

3.7 Conclusion

We found a decreased local dynamic stability when immediately transitioning from shod to barefoot running indicating an increase of control errors in the barefoot running. This transition resulted in biomechanical alterations of the running technique. We found an anterior shift of the foot strike patterns, increased cadence and decreased contact time and vertical displacement of the spine in the barefoot running. Larger changes in foot strike pattern during the transition from shod to barefoot running associated with higher system instability. It is suggested, that the decreased stability could arise in the stance phase and particularly in the push-off during barefoot running. The decreased stability might affect injury risk and performance.

3.8 Conflicts of interest

None.

3.9 Acknowledgements

We thank all participants for their commitment during the measurements. Further, we acknowledge Arno Schroll for his mathematical support in data analysis.

4 Third study – Short- and long-term effects of altered point of ground reaction force application on human running energetics

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4.1 Abstract

In the current study we investigated the effects of an acute and a gradual transition of the point of force application (PFA) from the rearfoot towards the fore of the foot during running, on the rate of metabolic energy consumption. We hypothesized that this shift would decrease the cost coefficient and lead to an improvement in the running economy. The participants were randomly assigned in two experimental and one control groups: a short-term intervention group (STI, N=17) performing two training sessions to achieve the transition to a more forward PFA, a long-term intervention group (LTI, N=10) performing a 14-week gradual transition to a more forward PFA and a control group (CG, N=11). Both experimental groups changed their PFA using a feedback-enhanced training protocol. Kinetic and kinematic parameters, local dynamic stability and oxygen consumption at two running velocities (2.5 and 3.0 m/s) were measured before and after the interventions. Both interventions induced a decrease ($p<0.001$) in the cost coefficient (i.e. energy required for a unit force, J/N) due to a more anterior PFA during running (STI: 12%, LTI: 11%), but led to a higher rate ($p<0.001$) of force applied to the ground (STI: 17%, LTI: 15.2%). Dynamic stability of running showed a significant ($p<0.001$) decrease in the STI (2.1%), but no differences ($p=0.673$) in the LTI. The rate of metabolic energy consumption increased in the

STI (p=0.028), but remained unchanged in the LTI (p=0.643). The control group did not show changes in any of the examined parameters. These results exhibit that the cost coefficient has successfully decreased following an alteration in the running technique towards a more anterior PFA. However, the positive effect of this change in the rate of metabolic energy consumption was counteracted by an increased rate of force generation due to a decreased contact time per step. The increased instability found during the short-term intervention and its neutralization after the long-term intervention indicates a role of motor control errors in the economy of running after acute alterations in habitual running execution.

4.2 Keywords

Lyapunov exponents, nonlinear dynamics, metabolic cost of locomotion, running economy, feedback training, effective mechanical advantage

4.3 Introduction

Endurance running performance depends on a complex interplay between a high maximal oxygen uptake, the ability to sustain a high percentage of VO_{2max} for long periods of time and the ability to move economically [100–102,84]. Running economy, which is defined as the rate of oxygen consumption per unit body mass when running at a constant velocity [78,100] or as energy cost of running expressed as the metabolic energy cost per body weight and per distance traveled [75,97] has been regularly accepted to highly determine endurance running performance [103–105]. Although numerous studies [78–81,84,205] tried to identify the physiological and biomechanical factors that affect the energy cost of running, only a few employed interventional designs to directly improve the energy cost of running [206,205,124,207,208].

It is reported that a higher Achilles tendon stiffness and a higher strength of the plantar flexor muscles are important properties of the human system affecting the energy cost of running [122,123]. Subsequent interventions based upon these observations found that a training protocol that increased the Achilles tendon stiffness and the muscle strength of the

plantar flexors led to improvements on the energy cost of running of approximately 5% [124]. Further, it has been suggested [124] that the training-induced alterations in stiffness and muscle strength might originate from a change of the effective mechanical advantages (EMA; i.e. ratio of the muscle moment arm to the moment arm of the ground reaction force [136]) within the lower limb (i.e. smaller EMA for the ankle and greater EMA for the knee joint). Compared to the knee extensor muscles, the human plantar flexor muscles have shorter fascicles and are metabolically less costly than long-fibred muscles in generating the same force (i.e. lower active muscle volume for the production of the same muscle force) [187]. Therefore, an alteration of the EMA within the lower limb would initiate a redistribution of the muscular output within the lower extremities and might explain the observed improvement in energy cost of running [124]. However, this hypothesis has not been investigated experimentally to date. From a biomechanical point of view, a shift of the point of ground reaction force application (PFA) during running from the rearfoot towards the fore of the foot would result in a longer moment arm of the ground reaction force at the ankle joint and in a shorter moment arm of the ground reaction force at the knee joint. Such a change would imply a smaller EMA for the ankle but a greater EMA for the knee joint.

Among numerous mammals including humans, there is evidence that the rate of metabolic energy consumption of running is proportional to the rate of force applied to the ground [106,108]. Kram and Taylor (1990) found a nearly constant cost coefficient (energy required for a unit force) across different animals and running speeds and tested the “cost of generating force” hypothesis (i.e. the cost of running is primarily determined by the cost of supporting weight and by the time course of force application). According to the formulated concept from Kram and Taylor (1990), the rate of metabolic energy consumption can be determined as the product of a constant factor (cost coefficient) and the rate of force applied to the ground. We argue that a redistribution of the muscular output within the lower limb during human running towards greater EMA at the knee joint and lower EMA at the ankle joint could decrease the cost coefficient. This is due to the less costly force generation of the plantar flexor muscles compared to the knee extensor muscles and, thus, affecting the rate of metabolic energy consumption. In the present study, we investigated the effects of an exercise based, feedback directed alteration of the PFA towards the fore of the foot on the cost coefficient during running.

Transition towards a more anterior PFA results in several biomechanical adjustments during running [187,188,209]. Employing and learning a novel locomotion strategy involves the central nervous system and can challenge the neuromuscular system [135,210]. Altered neuromechanical function while acute transition between running conditions can yield control errors and instabilities during running [164,211]. However, dynamic stability is required for effective and safe locomotion [30,24], while accurate neuromuscular control constitutes a determining factor of running performance [80]. Lyapunov's theory of dynamic stability assesses the sensitivity of a mechanical system to small perturbations [7,11] and is commonly adopted as a criterion for the occurrence of control errors during locomotion [47,32,192,212,48,175]. Alterations at the self-selected running strategy, such as the intended shift towards a more anterior PFA, may introduce control errors to the system especially in the learning phase. These control errors when transitioning from one running strategy to another could play an important role on the energy cost of running. However, long-term training can enhance the processing of information and execution of locomotion [31,189,213], through spatial, temporal and functional adjustments of movements [214,210,135] amending such control errors.

The objective of the present study was to understand the effects of an acute and a gradual change in the PFA towards the fore of the foot during running on the rate of metabolic energy consumption. Based on previous works regarding the EMA [136,137] and energetics of running [106–108] we hypothesized that this shift would decrease the cost coefficient and lead to an improvement in the running economy. Further, our second hypothesis was that the execution of a novel running strategy could induce instabilities and negatively affect the metabolic energy consumption and these could be alleviated by a long-term intervention training. The ability of our participants to perform the new technique was ensured through a custom made software with feedback information. We measured steady-state oxygen consumption to calculate the energy cost of running, the local dynamic stability as a measure of control errors and biomechanical parameters to determine the mechanisms governing the transition.

4.4 Methods

4.4.1 Experimental protocol

The current study employed 52 runners (>10 km/week and 2 running sessions/week) who gave informed consent to the study's procedures. In the study only runners that employed a habitually rearfoot strike (RFS) were included. To select them, all participants run in their preferred velocity for two minutes on a pressure plate equipped treadmill with their habitual running technique (120 Hz acquisition frequency; FDM-THM-S, zebris Medical GmbH, Germany). We identified the RFS runners using the algorithm of Santuz et al. (2016). The foot strike pattern FSP was numerically quantified through the strike index (i.e. the distance from the heel to the center of pressure at first impact, relative to total foot length) based on the recorded foot pressure distribution using a validated algorithm [184]. A RFS was considered one that provided a strike index lower than 1/3, a midfoot strike (MFS) one that provided values between 1/3 and 2/3 and a forefoot strike (FFS) one with values above 2/3 of the total foot length [193].

The participants were randomly divided into three groups; a short-term intervention group (STI: n=18; 5 female) a long-term exercise intervention group (LTI: n=17; 9 female) and a control group (CG: n=17; 12 female). Identical measurements were conducted before and after the interventions in all groups. All groups performed an identical pre- and a post-measurement. The measurement procedure consisted of the participants running in a pressure-plate equipped treadmill. Our participants ran at two different fixed velocities; 2.5 and 3.0 m/s after a short acclimatization period (one min) and for six minutes in each velocity. No visual, verbal or other feedback was provided during the measurements. Further, no instructions or introduction to the specific target of the study were given to the participants prior to the pre-measurements. None of the participants had any musculoskeletal or neuromuscular impairments at the time of the measurements or during the six months prior to them. The study was conducted in accordance to the local university ethical guidelines. All participants gave informed consent and the approval of the local ethics committee *(Humboldt-Universität zu Berlin)* was obtained.

With the STI we investigated the effect of acutely transitioning from a RFS into running employing a MFS. Following the baseline measurements, the participants were introduced to the aim of the study and performed a short-term feedback enhanced intervention (i.e. two

30-minute long sessions with a difference of two days). A session consisted of two parts. Firstly, the participants executed a short run on the treadmill trying to achieve a MFS running. Afterwards they visually inspected their foot pressure imprints through a proprietary pressure plate software (WinFDM-T v2.5.1, zebris Medical GmbH, Germany). They were then presented with the numerical value of their strike index and its comparison to previous trials, the force development during contact as well as their average pressure distribution of all steps at the first contact of the foot. A typical visual output from the custom developed software is presented in Figure 19. Secondly, they received verbal feedback from an experienced researcher. The researcher customized the verbal instructions to each participant with focus on: shifting their body weight forward and concentrate on the movement of the ankle joint. Simple physical exercises (i.e. lean forward and run against a rope; lean forward against a rope and sudden rope release) were introduced if necessary. This procedure was repeated as appropriate with focus on the visual cues by the proprietary and the custom software. To assure competence and ability to execute the new running technique effortlessly, the participants performed two similar 30-minute long sessions on the treadmill with feedback information regarding FSP. Post-measurements were conducted four days after the pre-measurements, with prior instruction to maintain the new MFS running technique but without any feedback information during the whole period of the six minutes per velocity. One participant was unable to maintain the new pattern for the whole period of the six minutes during the post-measurements and was excluded from our results (STI: n=17; 4 female).

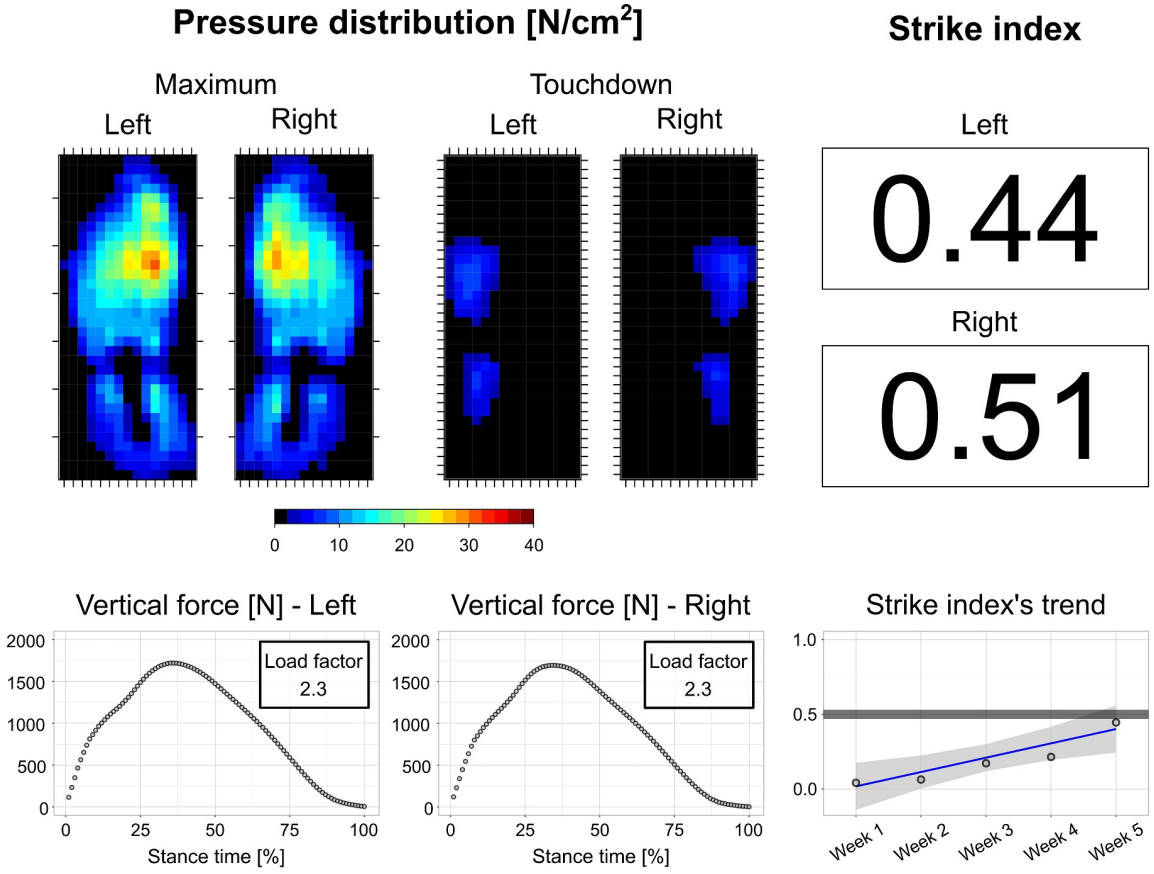

Figure 19. Exemplary visual output from the custom developed software. The figure depicts the averaged over all steps: pressure distribution at the timings of maximum pressure and at first contact (top left), the numerical force output during contact time (bottom left) and the strike index (top right). Further the current strike index was visualized in comparison to that of any previous trials; in grey the targeted value of 0.5 (bottom right).

The aim of the LTI was to investigate the effect of a long-term intervention targeting the transitioning from a RFS into running employing a MFS. The long-term feedback based intervention lasted 14 weeks in total and consisted of three parts. First, the participants were instructed to gradually exchange part of their training volume on their normal FSP with equal parts of MFS running. The amount was individually tailored to the participants who consulted with an experienced researcher. Secondly, they performed three times per week a session in addition to their normal training volume, which lasted ~30 minutes. The training included a set of exercises aiming to prepare and aid the transition into running with a MFS. The exercises focused at the lower extremities to prepare them for the added loading (i.e. step up with high knee, lunges landing on midfoot), on whole-body stability in order to

support the transition to a more forward leaning pose and on running technique with emphasis on MFS running simulation exercises. Thirdly, each week participants performed a specialized session (~30 min) in our lab. In this session, they received extensive verbal and visual cues on their running technique as we described in the training of the STI. Six participants dropped out due to time restrictions in performing the intervention and one due to injury, unrelated to the intervention program. Post-measurements were conducted one week after the completion of the exercise program in the remaining participants (n=10; 3 female). The participants were instructed prior to the post-measurements to keep the new MFS technique without any feedback information during the actual measurements for the whole six minutes in both velocities. Participants of the CG were instructed to maintain their training habits unaltered until the post-measurements, which took place 15 weeks after the baseline. Six participants dropped out due to time restrictions and did not participate in the post-measurements (n=11; 7 female).

4.4.2 Experimental setup

Two trials of 120 seconds were captured in each velocity. Both trials were captured amid the six-minute run on the treadmill. From the raw plantar pressure distribution values over time, we extracted: cadence, contact and flight time, average force per step, ground reaction forces and FSPs. To exclude any time dependent effect of the pressure plate sensors on the LTI and CG we measured overground ground reaction forces on a force plate (AMTI BP400600-2000, Watertown, USA) on a separate session and used these force values for subsequent analysis. We controlled for achieving exactly the same velocities (2.5 m/s and 3.0 m/s) as during treadmill running with the use of light barriers (velocity tolerance levels was set to 0.05 m/s). The average of three trials in each speed was used for subsequent calculations. All participants contacted the plate with the same foot (i.e. the right foot) in all trials.

During the treadmill trials, four high-speed video cameras (Flare 4M180-CCL, IO Industries Inc., Canada) operating at 170 Hz captured four reflective 14 mm-markers positioned on the spine [164]. Namely, the second, seventh, tenth, thoracic and the second lumbar vertebrae were recorded. The automated tracking was performed using dedicated software (Simi Motion 9.2.0, Simi Reality Motion Systems GmbH, Germany). The videos were synchronized with the pressure plate using an analogue signal triggered by the video capturing software (Simi

Grab 2.1.1, Simi Reality Motion Systems GmbH, Germany). A fourth order Butterworth 20 Hz low-pass filter was applied to the registered coordinates, maintaining the maximum dynamics of the system [163].

4.4.3 Local dynamic stability

Local dynamic stability was calculated through the maximum Lyapunov exponents (MLE). We calculated the MLE on the vertical axis of the clustered coordinate data of the four markers registered on the spine (i.e. on the averaged coordinates of the four markers) according to the procedure followed at a previous study [164]. In short, after identifying the maximum common steps of all participants in each group and all trials in the duration of 120 seconds, we extracted the corresponding data segment at each trial. This segment was then normalized to a uniform data length of ~18500 data points. We reconstructed the state space of the input one dimensional series through delay-coordinate embedding [13] as follows:

$$\boldsymbol{S(t)} = [z(t), z(t+\tau), \ldots, z(t+(m-1)\tau)], \quad (1)$$

with **S(t)** being the *m*-dimensional reconstructed state vector, z(t) the input 1D coordinate series, τ the time delay and *m* the embedding dimension. Time delays were selected based on the first minimum of the Average Mutual Information curve [18] and number of embedding dimensions through a Global False Nearest Neighbours analysis [21], with a threshold of one per thousand data points. Individually selected time delays were chosen by averaging the outcome delays of all individual time series for each of the participants [164]. For our data, *m*=3 was sufficient for all subjects, while τ ranged from 19 to 24 frames (~0.33 of average step). We then calculated the average divergence of each point's trajectory to its closest, employing the Rosenstein algorithm [68]. The MLE was calculated from the slopes of linear fits to the resulting average divergence curves on the frames equal to one step. The smaller the MLE, the more stably the system responds locally to small variations or perturbations.

4.4.4 Metabolic cost of running

Oxygen consumption (ml/min) during running was measured at both velocities (2.5 and 3.0 m/s) using an indirect calorimetry system (Metalyzer 3B, CORTEX Biophysik GmbH, Germany) with an acquisition frequency of ~0.5 Hz. Oxygen uptake was measured for six

minutes during which the researchers visually inspected and confirmed the respiratory exchange ratio to be <1.0. The last three minutes of each trial were averaged to calculate the oxygen consumption of each individual in each velocity. A fixed energy equivalent of 20.1 J ml^{-1} O_2 was used to convert measurements of oxygen consumption to rate of metabolic energy consumption [J/min] [215]. Further we determined the cost coefficient (c) according to Kram and Taylor (1990). Kram and Taylor (1990) found a constant cost coefficient (energy required for a unit force, J/N) across different animals and running velocities and evidenced that the rate of metabolic energy consumption ($\dot{E}$ $[W]$) of a running animal is proportional to the rate of force application on the ground (F_{rate} $[N/s]$). Therefore, the cost coefficient can be assessed by the following equations:

$$\dot{E} = c \cdot F_{rate} \Rightarrow c = \frac{\dot{E}}{F_{rate}}, \quad (2)$$

The rate of force generation was the quotient of the division of the average vertical ground reaction forces by the duration of the ground contact [106,107].

$$F_{rate} = \frac{\overline{F}_{vertical}}{t_{contact}}, \quad (3)$$

The oxygen consumption was normalized to body mass, while the rate of metabolic energy consumption was not. All raw data were post-processed using custom algorithms (Matlab 2014b, Mathworks Inc., United States; R version 3.1.2, R Core Team, Vienna, Austria).

4.4.5 Statistics

The effects of the short intervention (2 sessions) have been investigated with a repeated measures two-way ANOVA, with pre- and post-measurements and velocity as within-subjects factors. The effects of the long intervention (14 weeks) were tested using a repeated measures mixed-design ANOVA with pre- and post-measurements and velocity as within-subjects factors and group (LTI and CG) as between subject factor (SPSS v.24, International Business Machines Corp., USA). A Bonferroni-corrected *post-hoc* analysis was conducted in the case of a significant time effect or interaction of the factors time and intervention. To compare the anthropometric data between groups, we used a one-way ANOVA. The level of significance was set to $\alpha = 0.05$. Furthermore, to estimate the strength of potential alterations

of the investigated parameters following the exercise interventions, the effect size (d) was calculated. Values of $d < 0.2$ indicate small effect sizes, $0.2 \leq d < 0.8$ indicate medium sizes and $d \geq 0.8$ indicate large effect sizes [216]. To examine the relationship between investigated parameters (i.e. rate of metabolic energy consumption and rate of force generation) the Pearson correlation coefficient was used.

4.5 Results

Anthropometric data for the STI (n=17; age: 31 ± 4 years; height: 178 ± 9 cm; body mass: 73 ± 12 kg), LTI (n=10; age: 33 ± 5 years; height: 178 ± 8 cm; body mass: 71 ± 8 kg) and CG (n=11; age: 31 ± 3 years; height: 175 ± 9 cm; body mass: 69 ± 10 kg) presented no significant differences (age: p=0.431, height: p=0.611, body mass: p=0.729). Considering the baseline measurements (i.e. only the values obtained as pre-measurements) and including both investigated velocities and all three groups, the rate of metabolic energy consumption showed a high correlation with the rate of force generation (r=0.673, p<0.001, Figure 20).

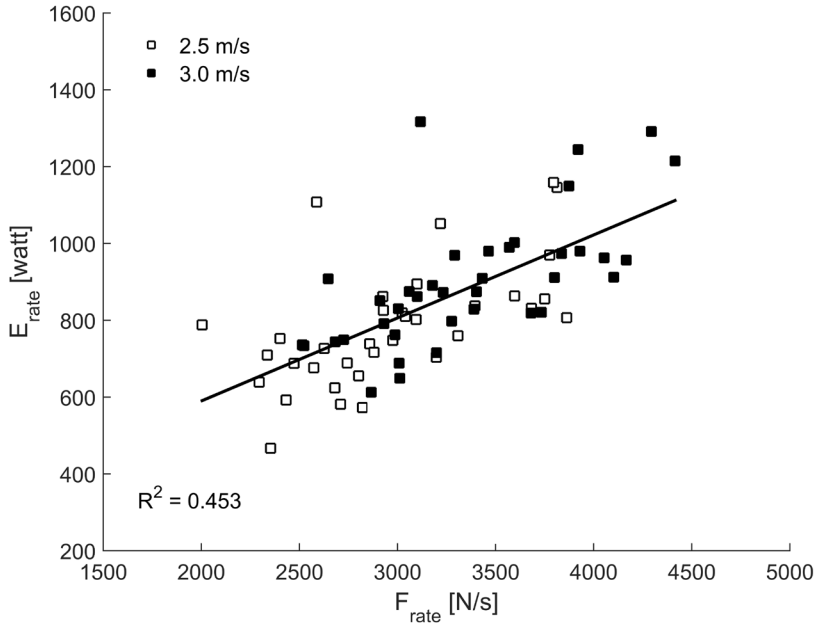

Figure 20. Relationship between rate of metabolic energy consumption (E_{rate}) and rate of force application on the ground (F_{rate}) for all investigated participants and running velocities.

4.5.1 Short-term intervention

After the two 30-minute long training sessions, all the participants of the STI were able to change their FSP from a RFS to a MFS. The average strike index increased significantly ($p<0.001$) in the post measurements at both investigated velocities (Table 5). The contact time presented significantly lower values ($p<0.001$), while the flight time significantly increased ($p<0.001$), in the post- compared to the pre-measurements (Table 5). Cadence remained unchanged before and after the training sessions ($p=0.961$, Table 5). The MLE values increased significantly ($p<0.001$) after the training sessions at both velocities (Figure 21). The cost coefficient decreased significantly ($p<0.001$) compared to the baseline measurements where the rate of force applied to the ground increased ($p<0.001$) after the intervention (Figure 21). The oxygen consumption and the rate of metabolic energy consumption increased significantly ($p=0.010$, Table 5 and $p=0.028$, Figure 21 respectively) after the training sessions.

Table 5. Strike index, contact time, flight time, cadence and oxygen consumption of the short-term intervention group (STI, n=17) over the two velocities (average values ± standard deviation).

	Velocity 2.5 m/s			Velocity 3.0 m/s		
Parameter	Pre	Post	d	Pre	Post	d
Strike index (dimensionless) †	0.09 ±0.05	0.53 ±0.12	4.84	0.08 ±0.05	0.51 ±0.16	3.65
Contact time (ms) †	309 ±30	289 ±26	0.72	279 ±23	262 ±18	0.82
Flight time (ms) †	64 ±27	85 ±23	0.83	84 ±22	99 ±20	0.73
Cadence (steps/min)	161.7 ±7.8	161.2 ±8.6	0.06	165.7 ±9.5	166.3 ±8.8	0.06
Oxygen consumption (ml/min/kg) †	32.5 ±4.6	33.5 ±5.6	0.20	38.0 ±4.8	38.9 ±5.7	0.17

†: Statistically significant time effect ($p<0.05$)

d: Cohen's Effect size

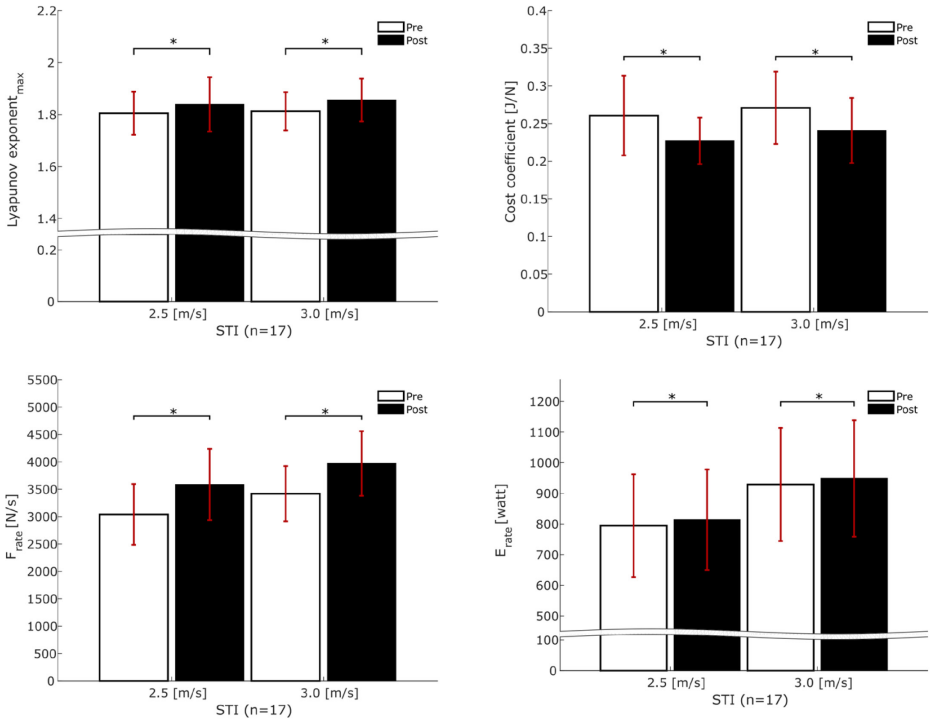

Figure 21. The maximum Lyapunov exponents, cost coefficient, rate of force development (Frate) and rate of metabolic energy consumption (Erate) presented for the short-term intervention group (STI), during running at 2.5 m/s and at 3.0 m/s, before and after the short term intervention.

***: Statistically significant differences (post-hoc analysis) between pre and post intervention values ($p<0.05$)**

4.5.2 Long-term intervention

All the participants of the LTI changed their FSP from a RFS to a MFS after the long-term (14 weeks) intervention. On the other hand, no participant of the CG changed their original FSP, with all of them maintaining a RFS before and after 14 weeks. For the strike index there was a time by group interaction ($p<0.001$). There was a significant ($p<0.001$) increase in the strike index for the LTI, but not in the CG ($p=0.277$, Table 6). Regarding contact and flight time there was a time by group interaction for both parameters ($p<0.001$ and $p=0.003$ respectively). After the intervention program, the LTI presented significantly lower contact time and significantly increased flight time (both $p<0.001$). No statistically significant differences (contact time: $p=0.292$, flight time: $p=0.561$) were observed in the control group (Table 6). Cadence and MLE did not show any significant time effect ($p=0.817$ and $p=0.673$ respectively) after the 14 weeks (Table 6, Figure 22).

The cost coefficient exhibited a time by group interaction (p=0.045). For the LTI the cost coefficient decreased significantly (p<0.001) compared to the pre-measurements, with no significant (p=0.416) changes observed in the CG (Figure 22). We also found a time by group interaction (p<0.001) for the rate of force generation. The rate of force generation was significantly higher in the post-measurements (p<0.001) in the LTI. The CG did not show any statistically significant (p=0.141) changes after the 14 weeks (Figure 22). The oxygen consumption (Table 6) and the rate of metabolic energy consumption (Figure 22) did not change in the LTI or the CG (p=0.599 and p=0.643) after the 14 weeks.

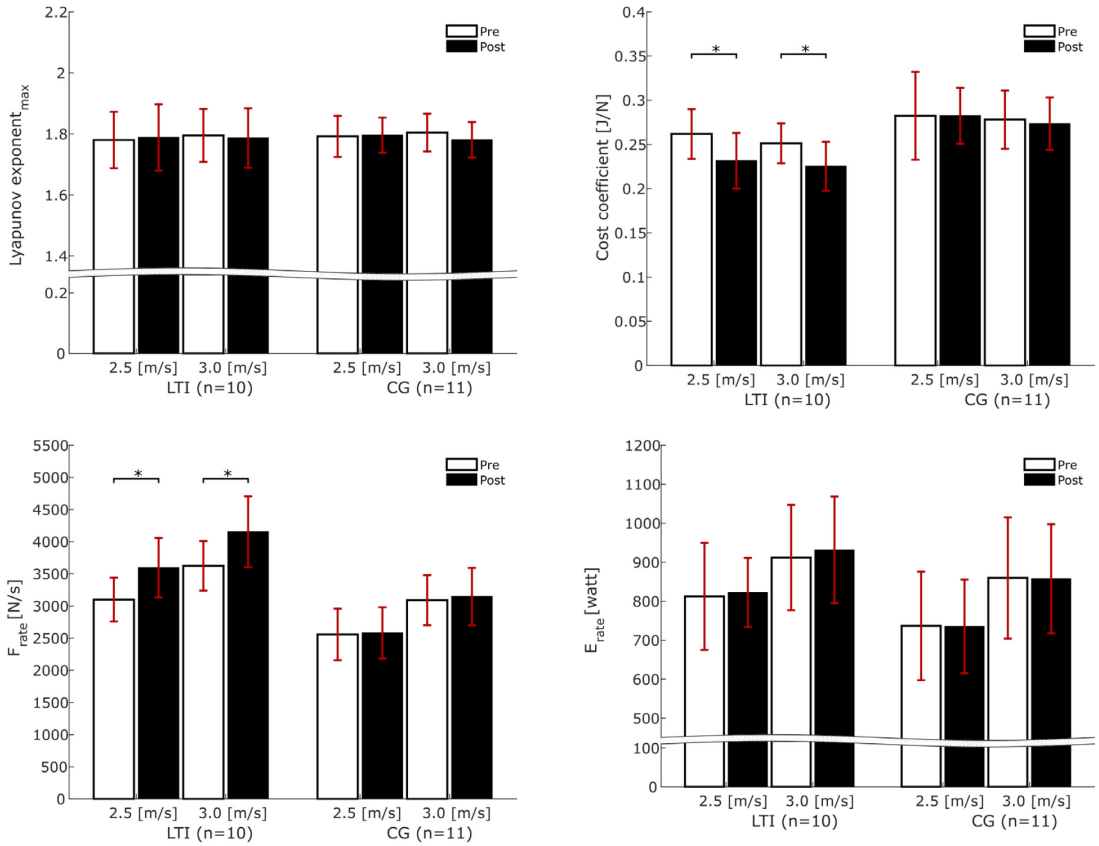

Figure 22. The maximum Lyapunov exponents, cost coefficient, rate of force development (Frate) and rate of metabolic energy consumption (Erate) presented for the long-term intervention group (LTI) and control group (CG), during running at 2.5 m/s and at 3.0 m/s, before and after the short term intervention.

***: Statistically significant differences (post-hoc analysis) between pre and post intervention values (p<0.05)**

Table 6. Strike index, contact time, flight time, cadence and oxygen consumption of the long-term intervention and the control group over the two velocities (average values ± standard deviation). Outcome parameters before (pre) and after (post) the intervention for the two study groups.

	Long-term intervention group (LTI, n=10)						Control Group (CG, n=11)					
	Velocity 2.5 m/s			Velocity 3.0 m/s			Velocity 2.5 m/s			Velocity 3.0 m/s		
Parameter	Pre	Post	d	Pre	Post	d	Pre	Post	d	Pre	Post	d
Strike index (dimensionless) †, #	0.09 ±0.03	0.51±0.16*	3.60	0.08 ±0.02	0.48 ±0.20 *	2.82	0.05 ±0.02	0.05 ±0.03	0.14	0.05 ±0.01	0.05 ±0.01	0.24
Contact time (ms) †, #	300 ±21	277 ±17 *	1.19	277 ±17	254 ±15 *	1.41	330 ±18	328 ±25	0.06	295 ±11	292 ±16	0.19
Flight time (ms) †, #	80 ±19	102 ±15 *	1.30	90 ±17	110 ±17 *	1.15	48 ±29	50 ±31	0.06	73 ±24	74 ±28	0.04
Cadence (steps/min)	158.7 ±11.7	158.4 ±7.7	0.03	164.4 ±11.8	165.5 ±10.1	0.10	159.5 ±10.6	159.0 ±8.6	0.05	163.7 ±11.4	164.3 ±10.3	0.05
Oxygen consumption (ml/min/kg)	34.0 ±2.6	34.7 ±1.5	0.29	38.3 ±2.4	39.1 ±3.5	0.28	31.2 ±4.0	31.1 ±2.4	0.03	36.9 ±3.7	36.8 ±2.8	0.03

†: Statistically significant time effect ($p<0.05$); #: Statistically significant time by group interaction ($p<0.05$)

*: Statistically significant differences (*post-hoc* analysis) between pre and post intervention values ($p<0.05$); d: Cohen's Effect size

4.6 Discussion

The present study investigated the effect of an acute and a gradual change in the PFA towards the fore of the foot during running on the rate of metabolic energy consumption, following a short-term (two sessions within one week) and a long-term (14 weeks) intervention. After completing the short- and long-term intervention both the STI and the LTI changed to a more forward PFA, which was evident by the increase in the strike index. The modified strike index resulted, indeed, in the decrease of the cost coefficient in both exercised groups during running. However, despite the reduction in the cost coefficient, the rate of metabolic energy consumption increased in the STI and remained unchanged in the LTI. Therefore, our first hypothesis (i.e. a shift towards a more forward PFA would decrease the cost coefficient and lead to an improvement in the running economy) has been rejected. On the other hand, the control errors induced by the acute change to the new running technique were alleviated by the long-term intervention, confirming our second hypothesis (i.e. a novel running strategy could induce instabilities, negatively affecting the energy cost of running and their alleviation by a long-term intervention training).

Although the cost coefficient of running in humans and other mammals is nearly constant across different velocities [106,108], it is well accepted that the muscle EMA may affect the cost coefficient of locomotion in humans [137] and animals [107,116,217] due to resulting changes in the active muscle volume. Biewener et al. (2004) demonstrated that the increased energy cost of running compared to walking originated by the lower EMA of the knee extensor muscles in running. Roberts et al. (1998a; 1998b) reported that the higher cost coefficient in birds compared to humans and quadrupedal mammals resulted by the greater ratio of muscle fiber length to muscle EMA. With the anterior shift of the PFA we intended a modification of the EMA within the lower extremities (i.e. smaller EMA for the ankle and greater EMA for the knee joint) and in this way a metabolically less costly force generation. There is indeed evidence in the literature for a redistribution of the muscular output in the lower extremities when runners move the PFA towards the fore of the foot [218,219]. A greater demand on the plantar flexor muscles and a lower demand of the knee extensor muscles is observed in runners who employ a FFS compared to runners who employ a RFS (Kulmala

et al., 2013; Stearne et al., 2014; Kuhman et al., 2016). Compared to the knee extensor muscles, the human plantar flexor muscles have shorter fascicles. Shorter muscle fascicles decrease the ratio of active muscle volume to muscle physiological cross sectional area by a given muscle force generation because typically muscle force is proportional to the active physiological cross sectional area [222]. This implies an energetic advantage for the plantar flexors and can affect the cost coefficient. Indeed, the decreased cost coefficient after the anterior shift of the PFA in both STI and LTI, evidences lower metabolic energy consumption per unit force in the post measurements. The decreased cost coefficient could be associated with a higher Previous studies provided evidence that the energy cost of running is primarily dependent on the cost of producing force in order to support the body weight [106,113,114]. It has been argued that the energy used by a unit volume of active muscle in a running animal is inversely proportional to the time needed to produce force [106], because faster muscle fibers, which are metabolically more expensive, have to be recruited [106,111,115].

In our study, the rate of force applied to the ground showed a high correlation to the rate of metabolic energy consumption during running supporting previous observations that the cost of producing force to support the body weight depends on the contact time [106,107,223,224]. Although cadence did not change in both groups, the anterior shift of the PFA led to shorter contact times and longer flight times while running. The shorter contact time at the same running velocity was the reason for the increased rate of force generation, which affects the rate of metabolic energy consumption. While running, the increased rate of force applied to the ground in the STI and the LTI means that both groups had to produce the necessary force to support body weight faster in each step and thus negatively affected the rate of metabolic energy consumption. Both interventions induced a decrease in the cost coefficient (STI: 12%, LTI: 11%) following an alteration in the running technique towards a more anterior PFA. However, the positive effect of this change in the rate of metabolic energy consumption was counteracted by an increased rate of force generation (STI: 17%, LTI: 15.2%) due to a decreased contact time per step. The inversely proportional changes of these two factors (i.e. cost coefficient and rate of force applied to the ground), which influence the rate of metabolic energy consumption, explain the absence of improvements in the rate of metabolic energy consumption during running after the interventions. Similar

reports and explanations have been provided by comparing the energy cost of locomotion between turkeys and dogs [217]. Although dogs showed a lower cost coefficient compared to turkeys, the higher rate of force applied to the ground neutralized the advantage of the cost coefficient and resulted to similar energetic cost of locomotion in trotting dogs and running turkeys [217].

Furthermore, in the STI we found an increase in the rate of metabolic energy consumption of 2.7% after the shift of the PFA towards the fore of the foot (i.e. worsening of the energy cost of running) despite an improvement in the cost coefficient. In the STI the MLE during running increased (2.1%) after the two-session exercise. The increased MLE corresponds to a more chaotic and unstable dynamical system [12,22] and indicates control errors in the neuromuscular control of locomotion [32,47]. Maintaining dynamic stability control is a prerequisite for successful execution of locomotion [24,31,133]. Learning new movements involves a number of interacting components which include detection, transmission and processing of sensory signals to appropriate motor commands [134,135] and therefore errors in the motor control and learning may affect the energy cost of locomotion. On uneven surfaces where stability is challenged [40], the rate of metabolic energy consumption is also increased [130]. Moreover, it has been suggested that 2% of the net energetic cost of running is attributed in maintaining stability in the lateral direction [225]. Studies on animals exhibited that animals often choose to optimize locomotion patterns to achieve increased stability, compromising energetically optimal mechanical work output and, thus, decreasing economy [132]. We can argue that the decreased stability after two exercise sessions provides evidence of motor control errors during running and leads to an additional cause of the increased rate of metabolic energy consumption in the STI.

After 14 weeks of exercise in which we trained the PFA towards the anterior of the foot, the MLE showed no differences compared to the pre-intervention values, indicating no control errors compared to the habitual running technique. Combining the findings of the short- and long-term interventions we provide evidence that exercise induced alteration of the habitual self-selected running technique leads to short-term instabilities challenging the energy cost of running. However, the initial instabilities were overcome by continued training of the new running technique. Following recent paradigms of renormalization of

motor control during skill acquisition [226,227], our results exhibit that we altered the self-chosen habitual running technique into a new one, successfully negating the instabilities and ensuring a renormalization of the motor output. Acute changes in the running technique cannot yield immediate improvements in running economy and the need for a gradual long-term intervention to overcome stability losses. Furthermore, as locomotion constitutes an emergent functional property [188], we observe an interplay between different mechanisms that affect and can have counterbalancing effects on the energy cost of running. This could be the reason behind discrepancies in the literature, since some studies suggest no benefit from a change in a more forward PFA [126,228], while others do [127]. Based on the results of the current study future interventions aiming to improve running economy could focus on changes in the PFA towards the fore of the foot during running, while maintaining similar contact times.

It has been shown that cost coefficients remains relatively constant across running velocities [106,229]. In our study and although the cost coefficient was changed after both, short- and long-term intervention, it did not show any differences between the two investigated running velocities. Furthermore, the high relationship between the rate of metabolic energy consumption and the rate of force application on the ground supported the formulated concept from Kram and Taylor (1990) that the cost of running is primarily determined by the cost of supporting weight and by the time course of force application. The assumption in this concept is that muscles are working at similar ranges of their force-velocity relationships at steady-state running speeds [108]. Recently, studies that measured the fascicle length of the *gastrocnemius medialis* [124] and *soleus* [230] reported similar shortening velocity of the fascicles in both muscles during different running velocities, evidencing a similar force-velocity potential of these muscles in a range of running speeds. To what extent more proximal muscles, as for example the knee extensors, show similar force-velocity potential by different running velocities remains to be seen in future research.

4.7 Conclusions

The present study found a decrease in the cost coefficient following an alteration in the running technique towards a more anterior PFA. This improvement was counterbalanced by an increased rate of force generation due to a decreased contact time per step. Our results indicate the existence of an additional mechanism that negatively affects the economy of running when the transition to an anterior PFA is acute. The increased instability during the acute transition and its neutralization after the long-term intervention provide evidence that motor control errors can have a role in the economy of running after acute alterations in habitual running execution.

4.8 Competing interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

4.9 Acknowledgements

The authors are grateful to the participants of the study for their commitment and interest during the measurements.

5 Main findings and conclusions

The current thesis endeavoured to provide an insight into the dynamic stability and the energetics during human locomotion. The background whereupon the calculation of the local dynamic stability is based was introduced, while the dynamic stability during locomotion and the differences in the exponent when considering different conditions, pathologies, age groups or methodologies was presented. Following, a background on the terminology and historical development of energy, together with insights on the significance and distinctness of human endurance running was presented. The part concluded with information on the energy cost of running and how this can be altered based on training interventions.

The ensuing experimental part was a venture to progress in the points and hypotheses presented at chapter 1.4. While in the recent years the popularity of the maximum Lyapunov exponent has increased substantially, there was scarce information on the reliability of the method. The first study was, thus, a methodological study (First study – The maximum Lyapunov exponent during walking and running: reliability assessment of different marker-sets). To address the hypotheses, a study design which compared two measurement blocks (i.e. two trials per day for three consecutive days per block) separated by two months on average was used. Following the reliability of six different marker-sets, deriving from markers on the trunk and both the walking and running conditions were explored. The results confirmed an increased reliability, when block measurements are used and that indeed different marker-sets exhibit different reliability values. Moreover, these results set the benchmark values for the reliability of measuring the dynamic stability using the maximum Lyapunov exponents during running.

Following, how an acute transition to a different condition - from shod to barefoot – would affect the resulting dynamic stability during running was examined (Second study – Transition from shod to barefoot alters dynamic stability during running). The results showed indeed that an acute transition from shod to barefoot running decreases the dynamic stability. It seems that disadvantages in the force generation that could possibly arise in the take-off phase of the running cycle might be a reason that hinders the dynamic stability. This effect could be also aided by the unfamiliar acute transition to the barefoot condition.

Lastly, a training intervention aiming at an improvement in running energetics was performed (Third study – Effects of an exercise induced alteration in the point of ground reaction force application on running energetics). In that study both interventions (i.e. a short- and a long-term intervention) succeeded in altering the cost coefficient, following the alteration of the running technique towards the fore of the foot. Although the decrease found would mean an improvement on the energy cost of running, it was counterbalanced by an increased rate of force generation due to a decreased contact time per step. Moreover, the increased instability (measured through the maximum Lyapunov exponents) during the provisional transition was neutralized after the long-term intervention. As such, a renormalization of the motor control output following the long-term intervention may be surmised[226,227]. These results evidence that motor control errors can have a role in the energy cost of running when acute alterations are happening in the habitual running execution. It is known that animals may optimize their locomotion patterns to achieve increased stability, often in disfavor of energetically optimal mechanical work output[132]. Although further research is necessary, a motor control prioritization trade-off might be possible. More specifically, the control of locomotion might be flexibly prioritized in a context-dependent manner.

5.1 Implications

5.1.1 Evaluation of the local dynamic stability during locomotion

An important aspect of the evaluation of the maximum Lyapunov exponent during locomotion is its reliability, in order to be used in research or other settings. More trials spread over more than one day (i.e. blocks of measurements), considerably improve the reliability of the measurement and should be considered in locomotion based study designs with increased demands of accuracy, be that walking or running. As such, the reliability, is acceptable in both walking and running for the detection of expected differences in experimental studies. Future experimental setups should also consider that the chosen marker-set influences the resulting exponent values. More than one marker may be preferable to ensure a high reliability in the running condition.

Another consideration arises, in the chosen parameters for the state-space reconstruction. Since each dynamical system is unique, in this thesis it was considered that every individual could be represented by a different set of parameters that would best reconstruct their data. Personalized chosen parameters (time delay τ and dimension *m*) -by averaging over all the trials performed per individual and accordingly reconstructing state spaces- were, thus, implemented. Such a strategy, being in strong accordance with nonlinear time series analysis theory[12,22], enabled reconstructions specific to the dynamical system without directly affecting the comparison between tasks.

More importantly, with the advent of increasingly powerful computation machines the maximum Lyapunov exponents can provide fast, relatively cheap and reliable information regarding the dynamic stability during locomotion. It is not unthinkable, but rather within our reach, to consider the local dynamic stability being computed and updated in real time. In such a case the information included in the calculation would be deriving from a standard amount of cycles as normally. However, each new analysis would disregard the last step in the calculation and start over including the next one, creating some sort of real time stability index. A real time per step stability index could be extremely useful for training purposes or as an early indicator for preventative measures in target populations (e.g. frail elderly).

5.1.2 Rehabilitation and performance optimization

As presented in chapter 1.2.2 the maximum Lyapunov exponents have been found in a number of studies to be important predictor of falls, with an increased value of the parameter being associated with a higher probability of falls[65,38,32,48]. However, this relationship has mostly been established during laboratory conditions[231]. Ambulatory measurements could provide valuable information on the amount and quality of daily-life activities and identify of individuals at risk of falls[232]. Recent advances in sensor sciences have increased the opportunities for accurate, wireless and long-lasting capturing of data. The use of accelerometers, combined with appropriate data analysis techniques can provide improved capabilities for such ambulatory measurements and monitor target populations at risk of falling[231]. While the accurate calculation of the maximum Lyapunov requires an increased amount of data points and consequently long-bouts of walking data, there have been attempts to improve the accuracy using multiple short-bouts of walking[69,231,232]. An

interesting idea for the field could be the concatenation of multiple short-bouts of steps in a single time-series and consequent analysis. A similar approximation may possibly be applied in experimental settings, in which the absence of multiple cycles in a given task is common. In such cases it is possible that concatenation of data deriving from different participants, could provide information on the dynamic stability which would be task specific.

Regarding performance optimization, the current thesis provided insights on how dynamic stability could have an important role when transitioning to a new running technique. Therefore, an important consideration should arise during trainings that attempt alterations in the habitual way of running. Further, while, several studies attempted alterations in the mechanics of running to enhance running performance, there is no consensus regarding an optimal running strategy. Locomotion constitutes an emergent functional property[188], and following a transition to a new running strategy it is almost impossible to alter only one biomechanical parameter, but rather several parameters are affected. Different neuromuscular and mechanical factors could contribute differently in the energy cost of running, often with counterbalancing effects. Future interventions could aim to improve running economy with multimodal approaches. For instance, based on the findings of the current thesis such an approach would be to target in maintaining the mechanical advantageous changes of the forward point of force application, while on the same time, maintaining similar contact times.

The maximum Lyapunov exponent has been recently used in clinical settings[48,60,139], and a new review included the measure to the ones suggested in standard gait analysis for neurological diseases assessment[233]. Based on two other reviews the maximum Lyapunov exponent has important potential in evaluating the fall risk in elderly[38,32]. However, as discussed in chapter 1.2.3 an important consideration when calculating the maximum Lyapunov exponent has been the different methodological approaches. Consensus on the methodological issues pertaining the calculation would be one step towards the widespread usage of the local dynamic stability in rehabilitation and training settings. Another step in the same direction would be the creation or open access to big data banks that could help

in the convergence towards some sort of normative values making the usage and interpretation of local dynamic stability easier.

5.1.3 Target priorities in movement

We know that motor control strategies are chosen in a context dependent manner, based on different criteria[131,132]. As seen in chapter 1.2, dynamic stability constitutes a crucial control priority for the central nervous system during locomotion and is a criterion for successful task execution. Moreover, we know that minimization of energy consumption (chapter 1.3) is a target priority for the system and constitutes a main criterion in locomotion. However, how the human central nervous system prioritizes between the different goals is unknown[234,235]. For instance, the introduction of a new running technique in the third study (chapter 4) of the current thesis, increased the rate of energy consumption, despite a mechanically advantageous technique and a decrease in the stability was found. As such a possible connection between these priorities has been established and can be examined further. The exact link between these two priorities is, however, obscure. Moreover, how other priorities (e.g. maneuverability) may come into play is unknown at the moment.

Recent achievements in experimental and computational tools could allow future studies to attack such long-standing complex problems in this field. Interdisciplinary approaches that would target all the levels of the human system and understand how muscles, sense organs, motor pattern generators, and brain interact to produce coordinated movement can be extremely useful in this task[236]. Recent studies attempted such combinations of methodologies to converge in improving our understanding of locomotion. For instance, an increased robustness is observed in face of perturbed locomotion and increased instability during walking and running[40]. Higher microstructural organization in a wide range of white matter tracts associates with increased stability[58] and adjusted gait parameters such as longer single support, less variability and larger strides[237,238]. On the other hand, reductions in executive functions may result in inaccurate control of limb movements and diminished feed-back that cause gait irregularity and instability[239]. In a promising new study novel relationships were established between gait metrics and the strength of within- or between- network functional connectivity[240]. Specifically, faster gait speed associated to stronger functional connectivity within the frontoparietal control

network, while those with less gait variability exhibited stronger negative functional connectivity between the dorsal attention network and the default network[240]. Be that as it may, the different target priorities and how the central nervous system interchangeably chooses between them and executes context depended locomotion, remains elusive. Such thought provoking concepts in the research frontiers could be the study of several more theses in the future.

References

1. Harari, Y. N. *Homo deus.* (Vintage, 2017).
2. Skoyles, J. R. Human balance, the evolution of bipedalism and dysequilibrium syndrome. *Med. Hypotheses* **66,** 1060–1068 (2006).
3. Bertram, J. E. A. *Understanding Mammalian Locomotion: Concepts and Applications*. (Wiley-Blackwell, 2016).
4. Schöner, G. & Kelso, J. A. Dynamic pattern generation in behavioral and neural systems. *Science* **239,** 1513–1520 (1988).
5. Davids, K., Glazier, P., Araújo, D. & Bartlett, R. Movement Systems as Dynamical Systems. *Sports Med.* **33,** 245–260 (2003).
6. Strogatz, S. H. *Nonlinear dynamics and chaos: with applications to physics, biology, chemistry, and engineering (Cambridge, MA*. (Westview Press, 1994).
7. Lyapunov, A. M. The general problem of the stability of motion. *Int. J. Control* **55,** 531–534 (1992).
8. Politi, A. Lyapunov exponent. *Scholarpedia* **8,** 2722 (2013).
9. Andronov, A. & Pontrjagin, L. Systèmes Grossiers. *Dokl Akad Nauk SSSR* **14,** 247–251 (1937).
10. Pugh, C. & Peixoto, M. M. Structural stability. *Scholarpedia* **3,** 4008 (2008).
11. Ihlen, E. A. F. *et al.* Fractional Stability of Trunk Acceleration Dynamics of Daily-Life Walking: Toward a Unified Concept of Gait Stability. *Front. Physiol.* **8,** 516 (2017).
12. Bradley, E. & Kantz, H. Nonlinear time-series analysis revisited. *Chaos* **25,** 097610 (2015).
13. Packard, N. H., Crutchfield, J. P., Farmer, J. D. & Shaw, R. S. Geometry from a Time Series. *Phys. Rev. Lett.* **45,** 712–716 (1980).
14. Takens, F. Detecting strange attractors in turbulence. in *Dynamical Systems and Turbulence, Warwick 1980* (eds. Rand, D. & Young, L.-S.) 366–381 (Springer, 1981). doi:10.1007/BFb0091924
15. Manabe, Y. & Chakraborty, B. A novel approach for estimation of optimal embedding parameters of nonlinear time series by structural learning of neural network. *Neurocomputing* **70,** 1360–1371 (2007).
16. Takens, F. Detecting strange attractors in turbulence. in *Dynamical Systems and Turbulence, Warwick 1980* (eds. Rand, D. & Young, L.-S.) 366–381 (Springer Berlin Heidelberg, 1981). doi:10.1007/BFb0091924
17. Sauer, T., Yorke, J. A. & Casdagli, M. Embedology. *J. Stat. Phys.* **65,** 579–616 (1991).
18. Fraser, A. M. & Swinney, H. L. Independent coordinates for strange attractors from mutual information. *Phys. Rev. A* **33,** 1134–1140 (1986).

19. Cover, T. M. & Suchergebnisse. *Elements of Information Theory*. (Wiley-Interscience, 2006).

20. Thomas, R. D., Moses, N. C., Semple, E. A. & Strang, A. J. An efficient algorithm for the computation of average mutual information: Validation and implementation in Matlab. *J. Math. Psychol.* **61,** 45–59 (2014).

21. Kennel, M., Brown, R. & Abarbanel, H. Determining embedding dimension for phase-space reconstruction using a geometrical construction. *Phys. Rev. A* **45,** 3403–3411 (1992).

22. Kantz, H. & Schreiber, T. *Nonlinear Time Series Analysis*. (Cambridge University Press, 2004).

23. May, R. M. Simple mathematical models with very complicated dynamics. *Nature* **261,** 459 (1976).

24. Patla, A. E. Strategies for dynamic stability during adaptive human locomotion. *IEEE Eng. Med. Biol. Mag.* **22,** 48–52 (2003).

25. Bramble, D. M. & Lieberman, D. E. Endurance running and the evolution of Homo. *Nature* **432,** 345–52 (2004).

26. Bernstein, N. *The co-ordination and regulation of movements*. (Pergamon-Press, 1967).

27. Ting, L. H. *et al.* Neuromechanical tuning of nonlinear postural control dynamics. *Chaos* **19,** (2009).

28. Ting, L. H. *et al.* Neuromechanical principles underlying movement modularity and their implications for rehabilitation. *Neuron* **86,** 38–54 (2015).

29. Reddy, P. G. *et al.* Brain State Flexibility Accompanies Motor-Skill Acquisition. *ArXiv170107646 Q-Bio* (2017).

30. Massion, J. Movement, posture and equilibrium: interaction and coordination. *Prog. Neurobiol.* **38,** 35–56 (1992).

31. Bohm, S., Mademli, L., Mersmann, F. & Arampatzis, A. Predictive and reactive locomotor adaptability in healthy elderly: A systematic review and meta-analysis. *Sports Med.* **45,** 1759–1777 (2015).

32. Bruijn, S. M., Meijer, O. G., Beek, P. J. & van Dieën, J. H. Assessing the stability of human locomotion: a review of current measures. *J. R. Soc. Interface R. Soc.* **10,** 20120999 (2013).

33. England, S. A. & Granata, K. P. The influence of gait speed on local dynamic stability of walking. *Gait Posture* **25,** 172–178 (2007).

34. Tad McGeer. Passive Dynamic Walking. *Int. J. Robot. Res.* **9,** 62–82 (1990).

35. Hobbelen, D. G. E. & Wisse, M. A Disturbance Rejection Measure for Limit Cycle Walkers: The Gait Sensitivity Norm. *Trans Rob* **23,** 1213–1224 (2007).

36. Kurz, M. J. & Stergiou, N. An artificial neural network that utilizes hip joint actuations to control bifurcations and chaos in a passive dynamic bipedal walking model. *Biol. Cybern.* **93,** 213–221 (2005).

37. Karssen, J. G. D. & Wisse, M. Fall detection in walking robots by multi-way principal component analysis. *Robotica* **27,** 249–257 (2009).

38. Hamacher, D., Singh, N. B., Van Dieën, J. H., Heller, M. O. & Taylor, W. R. Kinematic measures for assessing gait stability in elderly individuals: a systematic review. *J. R. Soc. Interface* **8,** 1682–1698 (2011).

39. Mehdizadeh, S. The largest Lyapunov exponent of gait in young and elderly individuals: A systematic review. *Gait Posture* **60,** 241–250 (2017).

40. Santuz, A., Ekizos, A., Eckardt, N., Kibele, A. & Arampatzis, A. Challenging human locomotion: stability and modular organisation in unsteady conditions. *Sci. Rep.* **8,** 2740 (2018).

41. Hak, L. *et al.* Speeding up or slowing down?: Gait adaptations to preserve gait stability in response to balance perturbations. *Gait Posture* **36,** 260–264 (2012).

42. Sloot, L. H. *et al.* Sensitivity of local dynamic stability of over-ground walking to balance impairment due to galvanic vestibular stimulation. *Ann. Biomed. Eng.* **39,** 1563–1569 (2011).

43. van Schooten, K. S. *et al.* Sensitivity of trunk variability and stability measures to balance impairments induced by galvanic vestibular stimulation during gait. *Gait Posture* **33,** 656–660 (2011).

44. McAndrew, P. M., Wilken, J. M. & Dingwell, J. B. Dynamic stability of human walking in visually and mechanically destabilizing environments. *J. Biomech.* **44,** 644–649 (2011).

45. Hak, L. *et al.* Walking in an Unstable Environment: Strategies Used by Transtibial Amputees to Prevent Falling During Gait. *Arch. Phys. Med. Rehabil.* **94,** 2186–2193 (2013).

46. Beurskens, R., Wilken, J. M. & Dingwell, J. B. Dynamic stability of superior vs. inferior body segments in individuals with transtibial amputation walking in destabilizing environments. *J. Biomech.* **47,** 3072–3079 (2014).

47. Dingwell, J. B. & Cusumano, J. P. Nonlinear time series analysis of normal and pathological human walking. *Chaos* **10,** 848–863 (2000).

48. Reynard, F., Vuadens, P., Deriaz, O. & Terrier, P. Could local dynamic stability serve as an early predictor of falls in patients with moderate neurological gait disorders? A reliability and comparison study in healthy individuals and in patients with paresis of the lower extremities. *PloS One* **9,** e100550 (2014).

49. Hoogkamer, W. *et al.* Toward new sensitive measures to evaluate gait stability in focal cerebellar lesion patients. *Gait Posture* **41,** 592–596 (2015).

50. Raz, N. *et al.* Regional brain changes in aging healthy adults: general trends, individual differences and modifiers. *Cereb. Cortex N. Y. N 1991* **15,** 1676–1689 (2005).

51. Papegaaij, S., Taube, W., Baudry, S., Otten, E. & Hortobágyi, T. Aging causes a reorganization of cortical and spinal control of posture. *Front. Aging Neurosci.* **6,** (2014).

52. Janssen, I., Heymsfield, S. B., Wang, Z. M. & Ross, R. Skeletal muscle mass and distribution in 468 men and women aged 18-88 yr. *J. Appl. Physiol.* **89,** 81–88 (2000).

53. Savelberg, H. H. C. M. & Meijer, K. The effect of age and joint angle on the proportionality of extensor and flexor strength at the knee joint. *J. Gerontol. A. Biol. Sci. Med. Sci.* **59,** 1120–1128 (2004).

54. Cruz-Jentoft, A. J. *et al.* Sarcopenia: European consensus on definition and diagnosis Report of the European Working Group on Sarcopenia in Older People. *Age Ageing* **39,** 412–423 (2010).

55. Savelberg, H. H. C. M., Fastenau, A., Willems, P. J. B. & Meijer, K. The load/capacity ratio affects the sit-to-stand movement strategy. *Clin. Biomech. Bristol Avon* **22,** 805–812 (2007).

56. Buzzi, U. H., Stergiou, N., Kurz, M. J., Hageman, P. A. & Heidel, J. Nonlinear dynamics indicates aging affects variability during gait. *Clin. Biomech.* **18,** 435–443 (2003).

57. Kang, H. G. & Dingwell, J. B. Effects of walking speed, strength and range of motion on gait stability in healthy older adults. *J. Biomech.* **41,** 2899–2905 (2008).

58. Bruijn, S. M., Van Impe, A., Duysens, J. & Swinnen, S. P. White matter microstructural organization and gait stability in older adults. *Front. Aging Neurosci.* **6,** 104 (2014).

59. Hamacher, D., Hamacher, D., Singh, N. B., Taylor, W. R. & Schega, L. Towards the assessment of local dynamic stability of level-grounded walking in an older population. *Med. Eng. Phys.* **37,** 1152–1155 (2015).

60. Terrier, P. & Reynard, F. Effect of age on the variability and stability of gait: a cross-sectional treadmill study in healthy individuals between 20 and 69 years of age. *Gait Posture* **41,** 170–174 (2015).

61. Hamacher, D., Hamacher, D., Singh, N. B., Taylor, W. R. & Schega, L. Towards the assessment of local dynamic stability of level-grounded walking in an older population. *Med. Eng. Phys.* (2015). doi:10.1016/j.medengphy.2015.09.007

62. American Geriatrics Society. Guideline for the Prevention of Falls in Older Persons. *J. Am. Geriatr. Soc.* **49,** 664–672 (2001).

63. Rubenstein, L. Z. Falls in older people: epidemiology, risk factors and strategies for prevention. *Age Ageing* **35,** ii37–ii41 (2006).

64. WHO. *Who Global Report on Falls: Prevention in Older Age*. (World Health Organization, 2007).

65. Hausdorff, J. M. Gait dynamics, fractals and falls: finding meaning in the stride-to-stride fluctuations of human walking. *Hum. Mov. Sci.* **26,** 555–589 (2007).

66. Gates, D. H. & Dingwell, J. B. Comparison of different state space definitions for local dynamic stability analyses. *J. Biomech.* **42,** 1345–1349 (2009).

67. Wolf, A., Swift, J. B., Swinney, H. L. & Vastano, J. A. Determining Lyapunov exponents from a time series. *Phys. Nonlinear Phenom.* **16,** 285–317 (1985).

68. Rosenstein, M. T., Collins, J. J. & De Luca, C. J. Reconstruction expansion as a geometry-based framework for choosing proper delay times. *Phys. Nonlinear Phenom.* **73,** 82–98 (1994).

69. Cignetti, F., Decker, L. M. & Stergiou, N. Sensitivity of the Wolf's and Rosenstein's algorithms to evaluate local dynamic stability from small gait data sets. *Ann. Biomed. Eng.* **40,** 1122–1130 (2012).

70. Rispens, S. M. *et al.* Identification of Fall Risk Predictors in Daily Life Measurements: Gait Characteristics' Reliability and Association With Self-reported Fall History. *Neurorehabil. Neural Repair* (2014). doi:10.1177/1545968314532031

71. Rispens, S. M. *et al.* A benchmark test of accuracy and precision in estimating dynamical systems characteristics from a time series. *J. Biomech.* **47,** 470–475 (2014).

72. Jordan, K., Challis, J. H., Cusumano, J. P. & Newell, K. M. Stability and the time-dependent structure of gait variability in walking and running. *Hum. Mov. Sci.* **28,** 113–128 (2009).

73. Rispens, S. M. *et al.* Consistency of gait characteristics as determined from acceleration data collected at different trunk locations. *Gait Posture* **40,** 187–192 (2014).

74. Kugiumtzis, D. State space reconstruction parameters in the analysis of chaotic time series — the role of the time window length. *Phys. Nonlinear Phenom.* **95,** 13–28 (1996).

75. di Prampero, P. E., Atchou, G., Brückner, J.-C. & Moia, C. The energetics of endurance running. *Eur. J. Appl. Physiol.* **55,** 259–266 (1986).

76. Prampero, P. E. di. The Energy Cost of Human Locomotion on Land and in Water*. *Int. J. Sports Med.* **07,** 55–72 (1986).

77. Morgan, D. W., Martin, P. E. & Krahenbuhl, G. S. Factors affecting running economy. *Sports Med.* **7,** 310–330 (1989).

78. Williams, K. R. & Cavanagh, P. R. Relationship between distance running mechanics, running economy, and performance. *J. Appl. Physiol. Bethesda Md 1985* **63,** 1236–1245 (1987).

79. Nummela, A., Keränen, T. & Mikkelsson, L. O. Factors related to top running speed and economy. *Int. J. Sports Med.* **28,** 655–661 (2007).

80. Bonacci, J., Chapman, A., Blanch, P. & Vicenzino, B. Neuromuscular adaptations to training, injury and passive interventions: implications for running economy. *Sports Med. Auckl. NZ* **39,** 903–921 (2009).

81. Barnes, K. R. & Kilding, A. E. Running economy: measurement, norms, and determining factors. *Sports Med. - Open* **1,** 8 (2015).

82. Lacour, J.-R. & Bourdin, M. Factors affecting the energy cost of level running at submaximal speed. *Eur. J. Appl. Physiol.* **115,** 651–673 (2015).

83. Moore, I. S. Is There an Economical Running Technique? A Review of Modifiable Biomechanical Factors Affecting Running Economy. *Sports Med.* **46,** 793–807 (2016).

84. Fletcher, J. R. & MacIntosh, B. R. Running economy from a muscle energetics perspective. *Front. Physiol.* **8,** 433 (2017).

85. Smith, C. *The Science of Energy: A Cultural History of Energy Physics in Victorian Britain*. (University of Chicago Press, 1999).

86. Smil, V. *Energy and Civilization: A History*. (The Mit Press, 2017).

87. Energy and Civilization. *MIT Press* Available at: https://mitpress.mit.edu/books/energy-and-civilization. (Accessed: 29th January 2018)

88. Hartman, M. A. & Spudich, J. A. The myosin superfamily at a glance. *J. Cell Sci.* **125,** 1627–1632 (2012).

89. Engelhardt, W. A. & Ljubimowa, M. N. Myosine and Adenosinetriphosphatase. *Nature* **144,** 668 (1939).

90. Huxley, A. F. & Niedergerke, R. Structural Changes in Muscle During Contraction: Interference Microscopy of Living Muscle Fibres. *Nature* **173,** 971 (1954).

91. Cooke, R. The Sliding Filament Model. *J. Gen. Physiol.* **123,** 643–656 (2004).

92. Spudich, J. Memories of Hugh E. Huxley (1924–2013). *Mol. Biol. Cell* **24,** 2769–2771 (2013).

93. Garland, T. The relation between maximal running speed and body mass in terrestrial mammals. *J. Zool.* **199,** 157–170 (1983).

94. Schmid, P. Functional Interpretation of the Laetoli Footprints. in *From Biped to Strider* 49–62 (Springer, Boston, MA, 2004). doi:10.1007/978-1-4419-8965-9_4

95. Carrier, D. R. *et al.* The Energetic Paradox of Human Running and Hominid Evolution [and Comments and Reply]. *Curr. Anthropol.* **25,** 483–495 (1984).

96. Heglund, N. C. & Taylor, C. R. Speed, stride frequency and energy cost per stride: how do they change with body size and gait? *J. Exp. Biol.* **138,** 301–318 (1988).

97. Margaria, R., Cerretelli, P., Aghemo, P. & Sassi, G. Energy cost of running. *J. Appl. Physiol.* **18,** 367–370 (1963).

98. Taylor, C. R., Schmidt-Nielsen, K. & Raab, J. L. Scaling of energetic cost of running to body size in mammals. *Am. J. Physiol.* **219,** 1104–1107 (1970).

99. Heglund, N. C., Fedak, M. A., Taylor, C. R. & Cavagna, G. A. Energetics and mechanics of terrestrial locomotion. IV. Total mechanical energy changes as a function of speed and body size in birds and mammals. *J. Exp. Biol.* **97,** 57–66 (1982).

100. Daniels, J. T., Yarbrough, R. A. & Foster, C. Changes in VO2max and Running Performance with Training. *Eur. J. Appl. Physiol.* **39,** 249–254 (1978).

101. Lucia, A. *et al.* Physiological characteristics of the best Eritrean runners — exceptional running economy. *Appl. Physiol. Nutr. Metab.* **31,** 530–540 (2006).

102. Foster, C. & Lucia, A. Running economy: the forgotten factor in elite performance. *Sports Med. Auckl. NZ* **37,** 316–319 (2007).

103. Conley, D. L. & Krahenbuhl, G. S. Running economy and distance running performance of highly trained athletes. *Med. Sci. Sports Exerc.* **12,** 357–360 (1980).

104. Joyner, M. J. Modeling: optimal marathon performance on the basis of physiological factors. *J. Appl. Physiol. Bethesda Md 1985* **70,** 683–687 (1991).

105. Daniels, J. & Daniels, N. Running economy of elite male and elite female runners. *Med. Sci. Sports Exerc.* **24,** 483 (1992).

106. Kram, R. & Taylor, C. R. Energetics of running: a new perspective. *Nature* **346,** 265–267 (1990).

107. Roberts, T. J., Kram, R., Weyand, P. G. & Taylor, C. R. Energetics of bipedal running. I. Metabolic cost of generating force. *J. Exp. Biol.* **201,** 2745–2751 (1998).

108. Kram, R. Muscular force or work: what determines the metabolic energy cost of running? *Exerc. Sport Sci. Rev.* **28,** 138–143 (2000).

109. Barclay, C. J. Energetics of contraction. *Compr. Physiol.* **5,** 961–995 (2015).

110. Bárány, M. ATPase activity of myosin correlated with speed of muscle shortening. *J. Gen. Physiol.* **50,** Suppl:197-218 (1967).

111. Rall, J. A. Energetic aspects of skeletal muscle contraction: implications of fiber types. *Exerc. Sport Sci. Rev.* **13,** 33–74 (1985).

112. Rome, L. C. Scaling of muscle fibres and locomotion. *J. Exp. Biol.* **168,** 243–252 (1992).

113. Taylor, C. R., Heglund, N. C., McMAHON, T. A. & Looney, T. R. Energetic cost of generating muscular force during running: a comparison of large and small animals. *J. Exp. Biol.* **86,** 9–18 (1980).

114. Taylor, C. R. Force development during sustained locomotion: a determinant of gait, speed and metabolic power. *J. Exp. Biol.* **115,** 253–262 (1985).

115. Alexander, R. M. & Ker, R. F. Locomotion. Running is priced by the step. *Nature* **346,** 220–221 (1990).

116. Biewener, A. A. Biomechanics of mammalian terrestrial locomotion. *Science* **250,** 1097–1103 (1990).

117. Cavanagh, P. R., Pollock, M. L. & Landa, J. A Biomechanical Comparison of Elite and Good Distance Runners. *Ann. N. Y. Acad. Sci.* **301,** 328–345 (1977).

118. Morgan, D. W., Martin, P. E. & Krahenbuhl, G. S. Factors affecting running economy. *Sports Med. Auckl. NZ* **7,** 310–330 (1989).

119. Fletcher, J. R., Esau, S. P. & MacIntosh, B. R. Economy of running: beyond the measurement of oxygen uptake. *J. Appl. Physiol.* **107,** 1918–22 (2009).

120. Balsalobre-Fernández, C., Santos-Concejero, J. & Grivas, G. V. Effects of Strength Training on Running Economy in Highly Trained Runners: A Systematic Review With Meta-Analysis of Controlled Trials. *J. Strength Cond. Res.* **30,** 2361–2368 (2016).

121. Berryman, N. *et al.* Strength Training for Middle- and Long-Distance Performance: A Meta-Analysis. *Int. J. Sports Physiol. Perform.* **13,** 57–63 (2018).

122. Arampatzis, A. *et al.* Influence of the muscle-tendon unit's mechanical and morphological properties on running economy. *J. Exp. Biol.* **209,** 3345–3357 (2006).

123. Fletcher, J. R., Esau, S. P. & MacIntosh, B. R. Changes in tendon stiffness and running economy in highly trained distance runners. *Eur. J. Appl. Physiol.* **110,** 1037–1046 (2010).

124. Albracht, K. & Arampatzis, A. Exercise-induced changes in triceps surae tendon stiffness and muscle strength affect running economy in humans. *Eur. J. Appl. Physiol.* **113,** 1605–1615 (2013).

125. Coetzer, P. *et al.* Superior fatigue resistance of elite black South African distance runners. *J. Appl. Physiol. Bethesda Md 1985* **75,** 1822–1827 (1993).

126. Gruber, A. H., Umberger, B. R., Braun, B. & Hamill, J. Economy and rate of carbohydrate oxidation during running with rearfoot and forefoot strike patterns. *J. Appl. Physiol.* **115,** 194–201 (2013).

127. Di Michele, R. & Merni, F. The concurrent effects of strike pattern and ground-contact time on running economy. *J. Sci. Med. Sport* **17,** 414–418 (2014).

128. Hak, L. *et al.* Walking in an Unstable Environment: Strategies Used by Transtibial Amputees to Prevent Falling During Gait. *Arch. Phys. Med. Rehabil.* **94,** 2186–2193 (2013).

129. Voloshina, A. S., Kuo, A. D., Daley, M. A. & Ferris, D. P. Biomechanics and energetics of walking on uneven terrain. *J. Exp. Biol.* **216,** 3963–3970 (2013).

130. Voloshina, A. S. & Ferris, D. P. Biomechanics and energetics of running on uneven terrain. *J. Exp. Biol.* **218,** 711–719 (2015).

131. Chiel, H. J., Ting, L. H., Ekeberg, Ö. & Hartmann, M. J. Z. The Brain in Its Body: Motor Control and Sensing in a Biomechanical Context. *J. Neurosci.* **29,** 12807–12814 (2009).

132. Daley, M. A. & Usherwood, J. R. Two explanations for the compliant running paradox: reduced work of bouncing viscera and increased stability in uneven terrain. *Biol. Lett.* **6,** 418–421 (2010).

133. Winter, D. A. *The biomechanics and motor control of human gait*. (University of Waterloo Press, 1987).

134. Wolpert, D. M., Goodbody, S. J. & Husain, M. Maintaining internal representations: the role of the human superior parietal lobe. *Nat. Neurosci.* **1,** 529–533 (1998).

135. Wolpert, D. M., Diedrichsen, J. & Flanagan, J. R. Principles of sensorimotor learning. *Nat. Rev. Neurosci.* **12,** 739 (2011).

136. Biewener, A. A. Scaling body support in mammals: limb posture and muscle mechanics. *Science* **245,** 45–48 (1989).

137. Biewener, A. A., Farley, C. T., Roberts, T. J. & Temaner, M. Muscle mechanical advantage of human walking and running: implications for energy cost. *J. Appl. Physiol.* **97,** 2266–2274 (2004).

138. Wurdeman, S. R., Myers, S. A., Jacobsen, A. L. & Stergiou, N. Adaptation and prosthesis effects on stride-to-stride fluctuations in amputee gait. *PloS One* **9,** e100125 (2014).

139. Reynard, F. & Terrier, P. Role of visual input in the control of dynamic balance: variability and instability of gait in treadmill walking while blindfolded. *Exp. Brain Res.* **233,** 1031–1040 (2015).

140. Hamacher, D., Törpel, A., Hamacher, D. & Schega, L. The effect of physical exhaustion on gait stability in young and older individuals. *Gait Posture* **48,** 137–139 (2016).

141. Wu, Y. *et al.* Effect of active arm swing to local dynamic stability during walking. *Hum. Mov. Sci.* **45,** 102–109 (2016).

142. Vieira, M. F. *et al.* Linear and Nonlinear Gait Features in Older Adults Walking on Inclined Surfaces at Different Speeds. *Ann. Biomed. Eng.* 1–12 (2017). doi:10.1007/s10439-017-1820-x

143. Chini, G. *et al.* Local Stability of the Trunk in Patients with Degenerative Cerebellar Ataxia During Walking. *The Cerebellum* **16,** 26–33 (2017).

144. Reynard, F. & Terrier, P. Determinants of gait stability while walking on a treadmill: A machine learning approach. *J. Biomech.* **65,** 212–215 (2017).

145. Wickstrom, J., Stergiou, N. & Kyvelidou, A. Reliability of center of pressure measures for assessing the development of sitting postural control through the stages of sitting. *Gait Posture* **56,** 8–13 (2017).

146. Kang, H. G. & Dingwell, J. B. Intra-session reliability of local dynamic stability of walking. *Gait Posture* **24,** 386–390 (2006).

147. van Schooten, K. S., Rispens, S. M., Pijnappels, M., Daffertshofer, A. & van Dieen, J. H. Assessing gait stability: the influence of state space reconstruction on inter- and intra-day reliability of local dynamic stability during over-ground walking. *J. Biomech.* **46,** 137–141 (2013).

148. Reynard, F. & Terrier, P. Local dynamic stability of treadmill walking: intrasession and week-to-week repeatability. *J. Biomech.* **47,** 74–80 (2014).

149. Rábago, C. A., Dingwell, J. B. & Wilken, J. M. Reliability and Minimum Detectable Change of Temporal-Spatial, Kinematic, and Dynamic Stability Measures during Perturbed Gait. *PloS One* **10,** e0142083 (2015).

150. Kang, H. G. & Dingwell, J. B. Effects of walking speed, strength and range of motion on gait stability in healthy older adults. *J. Biomech.* **41,** 2899–2905 (2008).

151. Bruijn, S. M., van Dieën, J. H., Meijer, O. G. & Beek, P. J. Statistical precision and sensitivity of measures of dynamic gait stability. *J. Neurosci. Methods* **178,** 327–333 (2009).

152. Mehdizadeh, S. & Sanjari, M. A. Effect of noise and filtering on largest Lyapunov exponent of time series associated with human walking. *J. Biomech.* **64,** 236–239 (2017).

153. Winter, D. A., MacKinnon, C. D., Ruder, G. K. & Wieman, C. Chapter 32 An integrated EMG/biomechanical model of upper body balance and posture during human gait. in *Progress in Brain Research* (eds. Allum, J. H. J., Allum-Mecklenburg, D. J., Harris, F. P. & Probst, R.) **97,** 359–367 (Elsevier, 1993).

154. Cromwell, R., Schurter, J., Shelton, S. & Vora, S. Head stabilization strategies in the sagittal plane during locomotor tasks. *Physiother. Res. Int.* **9,** 33–42 (2004).

155. Kang, H. G. & Dingwell, J. B. Dynamic stability of superior vs. inferior segments during walking in young and older adults. *Gait Posture* **30,** 260–263 (2009).

156. Dingwell, J. B. & Marin, L. C. Kinematic variability and local dynamic stability of upper body motions when walking at different speeds. *J. Biomech.* **39,** 444–452 (2006).

157. Bruijn, S. M., van Dieën, J. H., Meijer, O. G. & Beek, P. J. Is slow walking more stable? *J. Biomech.* **42,** 1506–1512 (2009).

158. Sejdić, E., Findlay, B., Merey, C. & Chau, T. The effects of listening to music or viewing television on human gait. *Comput. Biol. Med.* **43,** 1497–1501 (2013).

159. Terrier, P. & Dériaz, O. Kinematic variability, fractal dynamics and local dynamic stability of treadmill walking. *J. Neuroengineering Rehabil.* **8,** 12 (2011).

160. Wurdeman, S. R. & Stergiou, N. Temporal structure of variability reveals similar control mechanisms during lateral stepping and forward walking. *Gait Posture* **38,** 73–78 (2013).

161. Kang, H. G. & Dingwell, J. B. A direct comparison of local dynamic stability during unperturbed standing and walking. *Exp. Brain Res. Exp. Hirnforsch. Expérimentation Cérébrale* **172,** 35–48 (2006).

162. Treutwein, B. Adaptive psychophysical procedures. *Vision Res.* **35,** 2503–2522 (1995).

163. Sinclair, J., Taylor, P. J. & Hobbs, S. J. Digital filtering of three-dimensional lower extremity kinematics: an assessment. *J. Hum. Kinet.* **39,** 25–36 (2013).

164. Ekizos, A., Santuz, A. & Arampatzis, A. Transition from shod to barefoot alters dynamic stability during running. *Gait Posture* **56,** 31–36 (2017).

165. Portney, L. G. & Watkins, M. P. *Foundations of Clinical Research: Applications to Practice*. (Prentice Hall, 2009).

166. van Schooten, K. S. *et al.* Assessing Physical Activity in Older Adults: Required Days of Trunk Accelerometer Measurements for Reliable Estimation. *J. Aging Phys. Act.* (2013).

167. Syczewska, M., Öberg, T. & Karlsson, D. Segmental movements of the spine during treadmill walking with normal speed. *Clin. Biomech.* **14,** 384–388 (1999).

168. Cappellini, G., Ivanenko, Y. P., Poppele, R. E. & Lacquaniti, F. Motor patterns in human walking and running. *J. Neurophysiol.* **95,** 3426–3437 (2006).

169. Estep, A., Morrison, S., Caswell, S., Ambegaonkar, J. & Cortes, N. Differences in pattern of variability for lower extremity kinematics between walking and running. *Gait Posture* **60,** 111–115 (2018).

170. Moraiti, C., Stergiou, N., Ristanis, S. & Georgoulis, A. D. ACL deficiency affects stride-to-stride variability as measured using nonlinear methodology. *Knee Surg. Sports Traumatol. Arthrosc. Off. J. ESSKA* **15,** 1406–1413 (2007).

171. Moraiti, C. O., Stergiou, N., Vasiliadis, H. S., Motsis, E. & Georgoulis, A. Anterior cruciate ligament reconstruction results in alterations in gait variability. *Gait Posture* **32,** 169–175 (2010).

172. Lamoth, C. J. C., Ainsworth, E., Polomski, W. & Houdijk, H. Variability and stability analysis of walking of transfemoral amputees. *Med. Eng. Phys.* **32,** 1009–1014 (2010).

173. Wurdeman, S. R., Myers, S. A. & Stergiou, N. Transtibial amputee joint motion has increased attractor divergence during walking compared to non-amputee gait. *Ann. Biomed. Eng.* **41,** 806–813 (2013).

174. Look, N. *et al.* Dynamic stability of running: the effects of speed and leg amputations on the maximal Lyapunov exponent. *Chaos* **23,** 043131 (2013).

175. Kao, P.-C., Dingwell, J. B., Higginson, J. S. & Binder-Macleod, S. Dynamic instability during post-stroke hemiparetic walking. *Gait Posture* **40,** 457–463 (2014).

176. Terrier, P., Luthi, F. & Dériaz, O. Do orthopaedic shoes improve local dynamic stability of gait? An observational study in patients with chronic foot and ankle injuries. *BMC Musculoskelet. Disord.* **14,** 94 (2013).

177. Butler, R. J., Hamill, J. & Davis, I. Effect of footwear on high and low arched runners' mechanics during a prolonged run. *Gait Posture* **26,** 219–225 (2007).

178. Rothschild, C. E. Primitive running: a survey analysis of runners' interest, participation, and implementation. *J. Strength Cond. Res. Natl. Strength Cond. Assoc.* **26,** 2021–2026 (2012).

179. Lieberman, D. E. *et al.* Foot strike patterns and collision forces in habitually barefoot versus shod runners. *Nature* **463,** 531–535 (2010).

180. Tam, N., Astephen Wilson, J. L., Noakes, T. D. & Tucker, R. Barefoot running: an evaluation of current hypothesis, future research and clinical applications. *Br. J. Sports Med.* **48,** 349–55 (2014).

181. Perl, D. P., Daoud, A. I. & Lieberman, D. E. Effects of footwear and strike type on running economy. *Med. Sci. Sports Exerc.* **44,** 1335–1343 (2012).

182. Perkins, K. P., Hanney, W. J. & Rothschild, C. E. The risks and benefits of running barefoot or in minimalist shoes: a systematic review. *Sports Health* **6,** 475–480 (2014).

183. Franz, J. R., Wierzbinski, C. M. & Kram, R. Metabolic cost of running barefoot versus shod: Is lighter better? *Med. Sci. Sports Exerc.* **44,** 1519–1525 (2012).

184. Santuz, A., Ekizos, A. & Arampatzis, A. A pressure plate-based method for the automatic assessment of foot strike patterns during running. *Ann. Biomed. Eng.* **44,** 1646–1655 (2016).

185. Fleming, N., Walters, J., Grounds, J., Fife, L. & Finch, A. Acute response to barefoot running in habitually shod males. *Hum. Mov. Sci.* **42,** 27–37 (2015).

186. Kelly, L. A., Lichtwark, G. A., Farris, D. J. & Cresswell, A. Shoes alter the spring-like function of the human foot during running. *J. R. Soc. Interface R. Soc.* **13,** (2016).

187. Biewener, A. A. & Daley, M. A. Unsteady locomotion: integrating muscle function with whole body dynamics and neuromuscular control. *J. Exp. Biol.* **210,** 2949–2960 (2007).

188. Biewener, A. A. Locomotion as an emergent property of muscle contractile dynamics. *J. Exp. Biol.* **219,** 285–294 (2016).

189. Shadmehr, R., Smith, M. A. & Krakauer, J. W. Error correction, sensory prediction, and adaptation in motor control. *Annu. Rev. Neurosci.* **33,** 89–108 (2010).

190. Hoffman, S. E. *et al.* Dynamic in-vivo assessment of navicular drop while running in barefoot, minimalist, and motion control footwear conditions. *Gait Posture* **41,** 825–829 (2015).

191. Hamacher, D. *et al.* The reliability of local dynamic stability in walking while texting and performing an arithmetical problem. *Gait Posture* **44,** 200–203 (2016).

192. Terrier, P. & Reynard, F. To what extent does not wearing shoes affect the local dynamic stability of walking?: effect size and intrasession repeatability. *J. Appl. Biomech.* **30,** 305–309 (2014).

193. Cavanagh, P. R. & Lafortune, M. A. Ground reaction forces in distance running. *J. Biomech.* **13,** 397–406 (1980).

194. Rossignol, S., Dubuc, R. & Gossard, J.-P. Dynamic Sensorimotor Interactions in Locomotion. *Physiol. Rev.* **86,** 89–154 (2006).

195. Arampatzis, A., Karamanidis, K. & Brüggemann, G.-P. Adaptational phenomena and mechanical responses during running: effect of surface, aging and task experience. *Eur. J. Appl. Physiol.* **98,** 284–98 (2006).

196. Nunns, M., House, C., Fallowfield, J., Allsopp, A. & Dixon, S. Biomechanical characteristics of barefoot footstrike modalities. *J. Biomech.* **46,** 2603–2610 (2013).

197. Braunstein, B., Arampatzis, A., Eysel, P. & Brüggemann, G.-P. Footwear affects the gearing at the ankle and knee joints during running. *J. Biomech.* **43,** 2120–2125 (2010).

198. Rolian, C., Lieberman, D. E., Hamill, J., Scott, J. W. & Werbel, W. Walking, running and the evolution of short toes in humans. *J. Exp. Biol.* **212,** 713–721 (2009).

199. Carrier, D., Heglund, N. & Earls, K. Variable gearing during locomotion in the human musculoskeletal system. *Science* **265,** 651–653 (1994).

200. Arampatzis, A., Brüggemann, G. P. & Metzler, V. The effect of speed on leg stiffness and joint kinetics in human running. *J. Biomech.* **32,** 1349–1353 (1999).

201. Duysens, J. & Pearson, K. G. Inhibition of flexor burst generation by loading ankle extensor muscles in walking cats. *Brain Res.* **187,** 321–332 (1980).

202. Pearson, K. G. Role of sensory feedback in the control of stance duration in walking cats. *Brain Res. Rev.* **57,** 222–227 (2008).

203. Halvorsen, K., Eriksson, M. & Gullstrand, L. Acute effects of reducing vertical displacement and step frequency on running economy. *J. Strength Cond. Res. Natl. Strength Cond. Assoc.* **26,** 2065–2070 (2012).

204. Reilly, S. M., McElroy, E. J. & Biknevicius, A. R. Posture, gait and the ecological relevance of locomotor costs and energy-saving mechanisms in tetrapods. *Zoology* **110,** 271–289 (2007).

205. Moore, I. S., Jones, A. M. & Dixon, S. J. Mechanisms for improved running economy in beginner runners. *Med. Sci. Sports Exerc.* **44,** 1756–1763 (2012).

206. Lake, M. J. & Cavanagh, P. R. Six weeks of training does not change running mechanics or improve running economy. *Med. Sci. Sports Exerc.* **28,** 860 (1996).

207. Clansey, A. C., Hanlon, M., Wallace, E. S., Nevill, A. & Lake, M. J. Influence of tibial shock feedback training on impact loading and running economy. *Med. Sci. Sports Exerc.* **46,** 973–981 (2014).

208. Craighead, D. H., Lehecka, N. & King, D. L. A novel running mechanic's class changes kinematics but not running economy. *J. Strength Cond. Res.* **28,** 3137–3145 (2014).

209. Williams, D. S., McClay, I. S. & Manal, K. T. Lower Extremity Mechanics in Runners with a Converted Forefoot Strike Pattern. *J. Appl. Biomech.* **16,** 210–218 (2000).

210. Wise, S. P. & Willingham, D. T. Motor Skill Learning. in *Encyclopedia of Neuroscience* (ed. Squire, L. R.) 1057–1066 (Academic Press, 2009). doi:10.1016/B978-008045046-9.00774-9

211. Kelly, L. A., Farris, D. J., Lichtwark, G. A. & Cresswell, A. G. The influence of foot-strike technique on the neuromechanical function of the foot. *Med. Sci. Sports Exerc.* **50,** 98 (2018).

212. Terrier, P. & Dériaz, O. Non-linear dynamics of human locomotion: effects of rhythmic auditory cueing on local dynamic stability. *Front. Physiol.* **4,** 230 (2013).

213. Wolpert, D. M. & Miall, R. C. Forward models for physiological motor control. *Neural Netw. Off. J. Int. Neural Netw. Soc.* **9,** 1265–1279 (1996).

214. Wolpert, D. M. & Flanagan, J. R. Motor prediction. *Curr. Biol.* **11,** R729–R732 (2001).

215. Blaxter, K. L. (Kenneth L. *Energy metabolism in animals and man / Kenneth Blaxter, Kt*. (Cambridge University Press, 1989).

216. Cohen, J. *Statistical power analysis for the behavioral sciences*. (Routledge, 1988).

217. Roberts, T. J., Chen, M. S. & Taylor, C. R. Energetics of bipedal running. II. Limb design and running mechanics. *J. Exp. Biol.* **201,** 2753–2762 (1998).

218. Davis, I. S., Rice, H. M. & Wearing, S. C. Why forefoot striking in minimal shoes might positively change the course of running injuries. *J. Sport Health Sci.* **6,** 154–161 (2017).

219. Hamill, J. & Gruber, A. H. Is changing footstrike pattern beneficial to runners? *J. Sport Health Sci.* **6,** 146–153 (2017).

220. Kulmala, J.-P., Avela, J., Pasanen, K. & Parkkari, J. Forefoot strikers exhibit lower running-induced knee loading than rearfoot strikers. *Med. Sci. Sports Exerc.* **45,** 2306–2313 (2013).

221. Stearne, S. M., Alderson, J. a., Green, B. a., Donnelly, C. J. & Rubenson, J. Joint kinetics in rearfoot versus forefoot running: Implications of switching technique. *Med. Sci. Sports Exerc.* **46,** 1578–1587 (2014).

222. Haxton, H. A. Absolute muscle force in the ankle flexors of man. *J. Physiol.* **103,** 267–273 (1944).

223. Wright, S. & Weyand, P. G. The application of ground force explains the energetic cost of running backward and forward. *J. Exp. Biol.* **204,** 1805–1815 (2001).

224. Griffin, T. M., Roberts, T. J. & Kram, R. Metabolic cost of generating muscular force in human walking: insights from load-carrying and speed experiments. *J. Appl. Physiol. Bethesda Md 1985* **95,** 172–183 (2003).

225. Arellano, C. J. & Kram, R. The energetic cost of maintaining lateral balance during human running. *J. Appl. Physiol. Bethesda Md 1985* **112,** 427–434 (2012).

226. Makino, H., Hwang, E. J., Hedrick, N. G. & Komiyama, T. Circuit mechanisms of sensorimotor learning. *Neuron* **92,** 705–721 (2016).

227. Wenger, E., Brozzoli, C., Lindenberger, U. & Lövdén, M. Expansion and renormalization of human brain structure during skill acquisition. *Trends Cogn. Sci.* **21,** 930–939 (2017).

228. Ogueta-Alday, A., RodríGuez-Marroyo, J. A. & GarcíA-LóPez, J. Rearfoot Striking Runners Are More Economical Than Midfoot Strikers: *Med. Sci. Sports Exerc.* **46,** 580–585 (2014).

229. Hoyt, R. W., Knapik, J. J., Lanza, J. F., Jones, B. H. & Staab, J. S. Ambulatory foot contact monitor to estimate metabolic cost of human locomotion. *J. Appl. Physiol. Bethesda Md 1985* **76,** 1818–1822 (1994).

230. Lai, A. *et al.* In vivo behavior of the human soleus muscle with increasing walking and running speeds. *J. Appl. Physiol. Bethesda Md 1985* **118,** 1266–1275 (2015).

231. van Schooten, K. S., Rispens, S. M., Elders, P. J. M., van Dieën, J. H. & Pijnappels, M. Toward ambulatory balance assessment: estimating variability and stability from short bouts of gait. *Gait Posture* **39,** 695–699 (2014).

232. van Schooten, K. S. *et al.* Ambulatory fall-risk assessment: amount and quality of daily-life gait predict falls in older adults. *J. Gerontol. A. Biol. Sci. Med. Sci.* **70,** 608–615 (2015).

233. Vienne, A., Barrois, R. P., Buffat, S., Ricard, D. & Vidal, P.-P. Inertial Sensors to Assess Gait Quality in Patients with Neurological Disorders: A Systematic Review of Technical and Analytical Challenges. *Front. Psychol.* **8,** (2017).

234. Bertram, J. E. Gait as solution, but what is the problem? Exploring cost, economy and compromise in locomotion. *Vet. J. Lond. Engl. 1997* **198 Suppl 1,** e3-8 (2013).

235. Bertram, J. E. A. Locomotion: Why We Walk the Way We Walk. *Curr. Biol.* **25,** R795–R797 (2015).

236. Nishikawa, K. *et al.* Neuromechanics: an integrative approach for understanding motor control. *Integr. Comp. Biol.* **47,** 16–54 (2007).

237. Bhadelia, R. A. *et al.* Diffusion tensor imaging, white matter lesions, the corpus callosum, and gait in the elderly., Diffusion Tensor Imaging, White Matter lesions, the Corpus Callosum and Gait in the Elderly. *Stroke Stroke J. Cereb. Circ.* **40, 40,** 3816, 3816–3820 (2009).

238. Verlinden, V. J. A. *et al.* Tract-specific white matter microstructure and gait in humans. *Neurobiol. Aging* **43,** 164–173 (2016).

239. Yogev-Seligmann, G., Hausdorff, J. M. & Giladi, N. The role of executive function and attention in gait. *Mov. Disord. Off. J. Mov. Disord. Soc.* **23,** 329–342; quiz 472 (2008).

240. Lo, O.-Y. *et al.* Gait Speed and Gait Variability Are Associated with Different Functional Brain Networks. *Front. Aging Neurosci.* **9,** (2017).

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Declaration

Ich erkläre, dass ich die vorliegende Dissertation selbständig und nur unter Verwendung der angegebenen Hilfsmittel angefertigt habe. Alle Zitate sowie sinngemäße wörtliche Wiedergaben, die anderen Werken entnommen wurden, sind unter Angabe der Quelle kenntlich gemacht.

I hereby declare that I have completed this doctoral thesis independently. All the sources and aids I used to support my work were explicitly declared and listed or, where specified, literally quoted.